

No. 24-1365

**In the United States Court of Appeals
for the District of Columbia Circuit**

DOCTORS FOR DRUG POLICY REFORM; BRYON ADINOFF, DR.,

Petitioners

v.

DRUG ENFORCEMENT ADMINISTRATION; ANNE MILGRAM, IN HER OFFICIAL
CAPACITY AS ADMINISTRATOR OF THE UNITED STATES DRUG ENFORCEMENT
ADMINISTRATION,

Respondents

On Petition for Review of Orders of the Drug Enforcement Administration
(Oct. 28, 2024 and Nov. 25, 2024)

**PETITIONERS' APPENDIX
VOLUME 1 OF 6
APP.1 to APP.497**

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Dated: February 17, 2025

Respectfully submitted,

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UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

ORDER DENYING MOTION TO STAY HEARING PROCEEDINGS

On December 4, 2024, Doctors for Drug Policy Reform and Bryon Adinoff (collectively, D4DPR), an entity that is not a party to these proceedings, filed a motion seeking an indefinite stay of proceedings (Motion to Stay or MTS) so that it can pursue relief in the United States Court of Appeals for the District of Columbia (the Circuit Court). *See* Attachment 1 (M. Zorn, Petitioner); MTS at 1.

By way of procedural background, these are formal hearing proceedings being conducted in connection with a notice of proposed rulemaking (NPRM) issued by the United States Department of Justice (the Department) on May 21, 2024. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 44597, 44597 (2024). The NPRM proposes the transfer marijuana from Schedule I of the Controlled Substances Act (CSA) to Schedule III. *Id.* Following the publication of the NPRM in the Federal Register by the Department, in accordance with the Attorney General's direction therein, the DEA Administrator determined that in-person hearing proceedings would be appropriate and issued a General Notice of Hearing (GNoH) which, *inter alia*, set an early December commencement date. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 70148, 70148-49 (2024). Subsequently, based on correspondence filed with the Agency (but not furnished to this tribunal) the Administrator designated a subset of twenty-five (25) individuals and organizations (evidently culled from a larger group of requestors) to participate in the hearing (Designated Participants or DPs). The DPs were evidently each notified of their participation status by a separate email either before or simultaneous with the GNoH (also not furnished to the tribunal) MTS at 4. D4DPR was apparently not among those receiving invitations from the Administrator to participate in the hearing. *Id.*

Simultaneously with the Administrator's identification of the twenty-five (25) DPs, I was designated by the Administrator¹ to preside over the hearing proceedings, but was not involved in or apprised of the process utilized to render her DP selection. In an order dated November 19, 2024 (the Standing Order), based on submissions by the DPs, I made determinations regarding standing and inclusion in these proceedings by applying the statutory and regulatory guideposts supplied by Congress and the CSA and its implementing regulations. In the Standing Order, the overwhelming majority of DPs maintained their status as hearing participants, but standing assessments were reached regarding a future discretionary decision as to the potential weight to be assigned in the recommended decision. Standing Ord. at 7.

On November 13, 2024, D4DPR, a filed a motion with this tribunal bearing the caption "Non-Party D4DPR's Motion to Intervene and Request for Final Appealable Determination" (Motion to Intervene or MTI) seeking a written final order memorializing the decision that caused its lack of its own invitational email from the Administrator, as well as an order from this tribunal authorizing its inclusion among the DPs notwithstanding her decision. MTI at 4-5.

In an order (MTI Denial Order or MTIDO), dated November 21, 2024, this tribunal denied D4DPR's Motion to Intervene based on a lack of jurisdiction to review, modify, or reverse the Administrator's inclusion/exclusion decisions. MTIDO at 2-3. The MTIDO also explained that, notwithstanding D4DPR's expressed frustration with the lack of a written denial by the Administrator explaining her action (addressed, *infra*), that organization's lengthy recitation of how this formal rulemaking process would benefit from its input, the value of the organization or its potential witnesses does not circumscribe the entire universe of permissible considerations available to the Administrator.² *City of San Antonio v. Civil Aeronautics Board*, 374 F.2d 326, 329 (D.C. Cir. 1967) ("No principle [of] administrative law is more firmly established than that of agency control of its own calendar."). The Agency is endowed with the right to place reasonable limits on the number of participants in a given Administrative Procedure Act (APA) hearing. *Id.* As discussed, *supra*, this tribunal does not possess the requests by, or even the number of, persons who sought hearing participation. However large or small that number is, it would be illogical to expect any agency to blithely admit all comers from

¹ 21 C.F.R. § 1316.52.

² Contrary to D4DPR's contention in its Motion to Stay (MTS at 5), the MTIDO did not purport to adjudicate the Administrator's determination as "reasonable" or otherwise. MTIDO at 2.

everywhere. Proceedings would theoretically never reach a resolution. This tribunal has neither the authority nor the inclination to review or reverse the Administrator's attendance determinations, but the conclusion that she must have authority to discern who among the vast population of the United States can participate is inescapable. To be sure, thousands upon thousands of individuals and entities across the country could add value to the issues to be decided here, but they cannot all be included, and someone (in this case the Agency) must make that determination.

As discussed, *supra*, D4DPR has petitioned the Circuit Court to review the Administrator's election to dis-include the organization from the group of Designated Participants. MTS at 1; Attachment 1. Interestingly, the Motion to Stay represents that on November 25, 2024, D4DPR was served with a one-page document from the Agency explaining (albeit briefly) the decision to decline to extend an invitation to the hearing proceedings.³ MTS at 5.

As explained in the MTIDO, the Administrative Procedure Act and the CSA's implementing regulations (the Regulations) are unsupportive of D4DPR's request that I issue an order including what the Agency head excluded. As discussed, in the MTIDO, DEA administrative law judges (ALJs) are designated⁴ to handle a case by the Administrator. 21 C.F.R. § 1316.52. The ALJ's "functions ... commence upon his designation and terminate upon the certification of the record to the Administrator." *Id.* Thus, the time the DPs were selected preceded my authority to act on the case. Even more importantly, in the APA, Congress decreed that "[o]n appeal from or review of the [ALJ's recommended decision] the agency has all the powers which it would have in making the [recommended decision] ... except as it may limit the issues on notice or by rule." 5 U.S.C. § 557(b). Appeals flow *from the ALJ to the Administrator*, not the other way around. I have not been designated to review the Administrator's prehearing

³ This document was also not forwarded to this tribunal by the Agency.

⁴ Designation for a case is not synonymous with the appointment of the ALJ. To that end, the APA and the DEA regulations authorize the identification, recognition and inclusion of material facts in the administrative record by the taking of official notice. 5 U.S.C. § 556(e); *Attorney General's Manual on the Administrative Procedure Act* § 7(d) (1947); 21 C.F.R. § 1316.59(e). Official notice is herein taken of the following: (1) the undersigned was initially appointed as an ALJ on November 21, 2001, at and by the Social Security Administration; (2) on March 9, 2009, the undersigned was appointed as an ALJ by the then-DEA Administrator, Michele Leonhart; and (3) on October 25, 2018, under Attorney General Order 4315-2018, then-Attorney General Jefferson B. Sessions ratified and approved the DEA Administrator's prior ALJ appointment of the undersigned. To the extent any DP seeks to challenge the factual predicate of the official notice taken in this matter that party may file an appropriate motion no later than fifteen (15) days from the issuance of this order.

actions on this matter or the manner in which her DP decisions were reached, issued, or not issued.⁵ The Administrator exercised her discretion to fix the number of DPs to be included, and to expand that number would effectively overrule her decision and exceed the proper and logical role of the ALJ under the APA and the CSA.⁶ Accordingly, no action was (or could be) taken regarding the D4DPR's Motion to Intervene, and for similar reasons, the same is true of this Motion to Stay.⁷

⁵ See *SEC v. Chenery Corp.*, 318 U.S. 80, 87 (1943) (“The grounds upon which an administrative order must be judged are those upon which the record discloses that its action was based.”). As I have discussed in other orders, while the decision to include or exclude a party arguably bears the hallmarks of a final agency action (5 U.S.C. § 702; 21 U.S.C. § 877), the Court of Appeals for the Sixth Circuit is not altogether convinced that anything is really final and reviewable until the whole adjudication has run its course. *Miami-Luken, Inc. v. DEA*, 900 F.3d 738, 743 (6th Cir. 2018) (The court held that a subpoena decision is not rendered final merely because the agency’s highest authority issued the decision prior to an ultimate disposition of the case.). Under this view of things, there is nothing particularly troubling about the Administrator issuing her justification letter after the determination so long as it happens before the final (court-reviewable) order.

⁶ Admittedly, had the standing determination been deferred to await the action of the ALJ, matters would have been procedurally different and the Administrator could have exercised her unquestioned authority to review my ruling on the matter. But that is not the way the matter progressed.

⁷ Even assuming *arguendo* that the Motion to Stay was evaluated on the merits by this tribunal, it would likely produce a similarly unfruitful result. In its evaluations of motions to stay administrative proceedings, the Agency has adopted the following factors set forth in *Nken v. Holder* (the *Nken* Factors), *to wit*:

- (1) whether the stay applicant has made a strong showing that he is likely to succeed on the merits; (2) whether the [stay] applicant will be irreparably injured absent a stay; (3) whether issuance of the stay will substantially injure the other parties interested in the proceeding; and (4) where the public interest lies.

556 U.S. 418, 434 (2009); *Jennifer L. St. Croix, M.D.*, 86 Fed. Reg. 30494, 30495 (2021). Utilizing the *Nken* Factors here would not likely move the needle in D4DPR's direction for the relief it seeks. Regarding *Nken* Factor One (success on the merits), D4DPR's argument depends on acceptance of the fact that the Administrator's determination was *ultra vires* and/or arbitrary and capricious. MTS at 7-11. There is no indication in the NPRM that the Attorney General intended to contravene existing regulations by a definitive *sub silentio* determination to curtail the Administrator's delegated authority. Such a draconian interpretation cannot be made lightly. The United States District Court case cited by D4DPR (MTS at 7-8) merely upholds the authority of the Attorney General to appoint a special prosecutor and cabin the appointee's authority within the bounds of the appointing instrument. *United States v. Libby*, 429 F.Supp.2d 27, 40-43 (D.D.C. 2006). It would be unreasonable to conclude that the language in the NPRM was drafted as a deliberate pull-back of authority long ago delegated by regulation, and the *Libby* case does not support the broad reading of the Attorney General's intent urged by D4DPR here. Further, even D4DPR's own assessment of its advocacy objective is not within the scope of the NPRM to move marijuana to Schedule III, but rather seeks to move it to some other, less restrictive schedule. MTS at 14-15; MTI at 1. It is thus beyond the scope of NPRM. Neither does *Nken* Factor Two (irreparable injury) provide assistance to D4DPR's cause here. To the extent that D4DPR's alleged harm to itself stems from its inability to present its views to the Agency, it is helpful to remember there was an extensive comment submission period set forth in the NPRM where that could have been done. 89 Fed. Reg. at 44597-98. Irreparable injury, even under the authority cited by D4DPR (MTS at 18-19) in support of the relief it seeks, requires, in no uncertain terms that “the injury must be both certain and great [and] actual and not theoretical.” *Wisconsin Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985). To the extent that it complains that the irreparable nature of its harm stems from a decision that was issued after the Administrator has made a final decision, or as the MTS put it, after “the cake has been baked” (MTS at 19), not only did D4DPR have the opportunity to submit comments that must be analyzed and incorporated into the final rule, but the DPs who are participating in the hearing are likely provide no shortage of highly-qualified expert opinions. Further, as discussed, *supra*, at least one court has determined that decisions rendered by an agency head during the

Accordingly, no action can or will be taken on the petition of this non-Designated Participant for a stay of proceedings.⁸

Dated: December 5, 2024

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JOHN J. MULROONEY, II
Chief Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on December 5, 2024 caused a copy of the foregoing to be delivered to the following recipients: (1) Julie L. Hamilton, Esq., Counsel for the Government, via email at Julie.L.Hamilton@dea.gov; James J. Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; Jarrett T. Lonich, Esq., Counsel for the Government, via email at jarrett.t.lonich@dea.gov; and S. Taylor Johnston, Esq., Counsel for the Government, via email at stephen.t.johnston@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington, Esq., Counsel for Village Farms International, via email at spennington@porterwright.com; and Tristan Cavanaugh, Esq., Counsel for Village Farms International, via email at tcavanaugh@porterwright.com; (4) Nikolas S. Komyati, Esq., Counsel for National Cannabis Industry Association, via email at nkomyati@foxrothschild.com; William Bogot, Esq., Counsel for National Cannabis Industry

pendency of APA proceedings may be interlocutory. *Miami-Luken*, 900 F.3d at 743. Importantly, a review of *Nken* Factors Three (injury to other parties) and Four requires a pragmatic evaluation of the relief actually being sought here. D4DPR seeks an indefinite stay so that the Circuit Court can review the Agency's hearing participation process. The APA hearing date is currently scheduled for January 21, 2025, the date that the Court of Appeals has fixed for D4DPR's initial submissions. Attachment 1 at 2. It is not altogether clear what D4DPR's representations that it "intends to take all reasonable steps to reduce the length of delay, including by seeking expedited review in [the Circuit Court]" really does (or could) mean. MTS at 20. The Circuit Court manages a busy docket. The most that D4DPR could hope for is a fair and timely consideration of its motion to expedite, along with similar motions filed by a multitude of other litigants. If ultimately successful in its litigation before that court, any relief granted in this petitioner's favor will almost undoubtedly involve the reversal of all actions related to the designation of DPs by the Agency and the Department. Under this success metric, the process will need to start again at square one. Invitations for hearing and participation requests will need to be rewritten and republished in the Federal Register with appropriate waiting times and supplemental instructions as to the status of those DPs selected in the Agency's initial efforts. The work of all concerned will be repeated. The Agency will certainly be called upon to review a potentially massive number of new (and old) submissions with detailed statements of position and arguments for standing. And all that will occur *after* the Circuit Court issues its decision on the process. The restarted process will then likely commence with a lengthy APA hearing that potentially will seat even more designated participants. After the *new* process is complete, the Agency will issue a final order that is *then* subject to appeal in the courts. To blithely assert that the stay requested here will have no cognizable impact on the Designated Participants or the members of the public who have long been anticipating an adjudication on these issues, may prove unpersuasive to say the least. Thus, while this order holds that this tribunal is without authority to rule on the Motion for Stay (or any other motion) filed by this non-DP, even if its Motion were to be considered, a thoughtful evaluation of the relief under the *Nken* Factors would likely militate in favor of its denial.

⁸ Naturally, any order provided by the Circuit Court will be expeditiously and scrupulously adhered to by this tribunal.

Association, via email at wbogot@foxrothschild.com; and Khurshid Khoja, Esq., Counsel for National Cannabis Industry Association, via email at khurshid@greenbridgelaw.com; (5) John Jones and Dante Picazo for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (6) Andrew J. Kline, Esq., Counsel for Hemp for Victory, AKline@perkinscoie.com; and Abdul Kallon, Esq., Counsel for Hemp for Victory, via email at and AKallon@perkinscoie.com; (7) Shanetha Lewis for Veterans Initiative 22, via email at info@veteransinitiative22.com; (8) Kelly Fair, Esq., Counsel for The Commonwealth Project, via email at Kelly.Fair@dentons.com; (9) Rafe Petersen, Esq., Counsel for Ari Kirshenbaum, via email at Rafe.Petersen@hklaw.com; (10) David G. Evans, Esq., Counsel for Cannabis Industry Victims Educating Litigators, Community Anti-Drug Coalitions of America, Phillip Drum, Kenneth Finn, International Academy on the Science and Impacts of Cannabis, and National Drug and Alcohol Screening Association, via email at thinkon908@aol.com; (11) Patrick Philbin, Esq., Counsel for Smart Approaches to Marijuana, via email at pphilbin@torridonlaw.com; and Chase Harrington, Esq., Counsel for Smart Approaches to Marijuana, via email at charrington@torridonlaw.com; (12) Stephanie E. Masker, Esq., Counsel for National Transportation Safety Board, via email at stephanie.masker@ntsb.gov; (13) Eric Hamilton, Esq., Counsel for the State of Nebraska, via email at eric.hamilton@nebraska.gov; and Zachary Viglianco, Esq., for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (14) Gene Voegtlin for International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (15) Gregory J. Cherundolo for Drug Enforcement Association of Federal Narcotics Agents, via email at executive.director@afna.org; (16) Reed N. Smith, Esq., Counsel for the Tennessee Bureau of Investigation, via email at Reed.Smith@ag.tn.gov; and Jacob Durst, Esq., Counsel for Tennessee Bureau of Investigation, via email at Jacob.Durst@ag.tn.gov; and (17) Matthew Zorn, Esq., Counsel for OCO *et al.*, and Counsel for Doctors for Drug Policy Reform and Bryon Adinoff, via email at mzorn@yettercoleman.com; abrumbaugh@yettercoleman.com.

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Quinn Fox
Staff Assistant to the Chief Judge
Office of Administrative Law Judges



U.S. Department of Justice
Drug Enforcement Administration

Office of the Administrator

Springfield, VA 22152

October 28, 2024

Hon. John J. Mulrooney, II
Chief Administrative Law Judge
Office of Administrative Law Judges
8701 Morrisette Drive
Springfield, VA 22152

Dear Chief Judge Mulrooney,

On May 21, 2024, the Department of Justice published a notice of proposed rulemaking (NPRM) to transfer marijuana from schedule I of the Controlled Substances Act (CSA) to schedule III of the CSA. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 44597 \(May 21, 2024\)](#). Upon review of the requests for hearing on the NPRM, I authorized a hearing to be conducted in accordance with the Administrative Procedure Act (APA), the CSA, and the Drug Enforcement Administration (DEA) regulations. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 70148 \(Aug. 29, 2024\)](#).

Pursuant to my authority under the CSA and DEA regulations, I reviewed the requests for a hearing under [21 CFR 1308.44\(a\)](#) and [1316.47](#), and the requests to participate under [21 CFR 1308.44\(b\)](#) and [1316.48](#), and I have determined that the following will be participants at the hearing:

1. Village Farms International Inc.
Shane Pennington of Porter Wright, spennington@porterwright.com
2. National Cannabis Industry Association
Aaron Smith, CEO and Co-Founder, and Michelle Rutter Friberg, Director of Government Relations, aaron@thecannabisindustry.org and michelle@thecannabisindustry.org
3. American Academy of Hospice and Palliative Medicine
Dr. Chad Kollas, MD, wchill@aahpm.org
4. Cannabis Bioscience International Holdings
John Jones, Treasurer and Director, ir@cbih.net

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LAW JUDGES

5. Hemp for Victory
Robert Head, Dr. Corey Burchman, Dr. Darinia Douchi, and Victor Bohm,
robert@bluecordfarms.com
6. Cannabis Ombudsman, State of Connecticut
Erin Gorman Kirk, Erin.Kirk@ct.gov
7. Massachusetts Cannabis Advisory Board
Ellen Brown, Research Subcommittee Chair, ellen@greenpathtraining.com
8. Veterans Initiative 22
Shanetha Lewis, Executive Director, info@veteransinitiative22.com
9. The Doc App. DbA, My Florida Green
Nicholas Garulay, President and CEO, and Jason Castro, Inhouse Counsel,
jasoncastro@myfloridagreen.com
10. The Commonwealth Project
Katy Green, kag@platinumadvisors.com
11. Saint Michael's College
Ari Kirshenbaum, PhD, Professor of Psychology,
mslade@cannabispolicyconsulting.com
12. National Drug and Alcohol Screening Association (NDASA)
Jo McGuire, jomcguire@ndasa.com
13. Smart approaches to Marijuana (SAM)
Patrick Philbin, pphilbin@torridonlaw.com
14. International Academy on the Science and Impact of Cannabis
Roneet Lev, roneetlev@gmail.com
15. Cannabis Industry Victims Educating Litigators
David Evans, Sr. Counsel, thinkon908@aol.com
16. Kenneth Finn, MD, kfinn@springsrehab.net
17. National Transportation Safety Board (NTSB)
Jennifer Homendy, Chair, ExecutiveSecretariat@ntsb.gov and
correspondence@ntsb.gov
18. Phillip Drum, Pharm D, phillipdrum@comcast.net

19. State of Nebraska
Attorney General Mike Hilgers, zachary.viglianco@nebraska.gov
20. International Association of Chiefs of Police (IACP)
voegtlin@theiacp.org
21. Drug Enforcement Association of Federal Narcotics Agents (DEAFNA)
marshallfisher@rocketmail.com
22. American College of Occupational and Environmental Medicine (ACOEM)
Natalie P. Hartenbaum, occumedix@comcast.net cc: craig@acoem.org
23. Community Anti-Drug Coalitions of America (CADCA)
Sue Thau, cdoarn@cadca.org
24. Tennessee Bureau of Investigation (TBI)
kim.litman@tbi.tn.gov
25. National Sheriff's Association
sheriffskinner@collincountytx.gov and ykaraman@sheriffs.org

Further, an Administrative Law Judge (ALJ) is now designated to preside over the hearing. The ALJ's functions commence upon this designation. *See* [21 CFR 1316.52](#). The designated ALJ will have powers necessary to conduct a fair hearing, to take all necessary action to avoid delay, and to maintain order. *Id.* The ALJ's authorities include the power to hold conferences to simplify or determine the issues in the hearing or to consider other matters that may aid in the expeditious disposition of the hearing; require parties to state their position in writing; sign and issue subpoenas to compel the production of documents and materials to the extent necessary to conduct the hearing; examine witnesses and direct witnesses to testify; receive, rule on, exclude, or limit evidence; rule on procedural items; and take any action permitted by the presiding officer under DEA's hearing procedures and the APA. *Id.*

Sincerely,



Anne Milgram
Administrator



U. S. Department of Justice
Drug Enforcement Administration
8701 Morrisette Drive
Springfield, Virginia 22152

www.dea.gov

Bryon Adinoff
812 S Gaylord St.
Denver, CO 80209
mzorn@yettercoleman.com
adinoff@d4dpr.org

Dear Bryon Adinoff,

This is in response to your request, for a hearing and/or to participate in a hearing, to the Drug Enforcement Administration (DEA) regarding the notice of proposed rulemaking (NPRM) to transfer marijuana from schedule I of the Controlled Substances Act (CSA) to schedule III of the CSA. See Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 44597 (May 21, 2024) and 89 FR 70148 (Aug. 29, 2024).

Upon review and careful consideration, DEA has determined that the request did not sufficiently establish that you are an “interested person” under DEA regulations and/or the request did not sufficiently state with particularity the relevant evidence on a material issue of fact that you intended to present during the hearing. See 21 CFR 1300.01(b), 1308.44(a), 1308.44(b), 1316.47, 1316.48; see also Placement of Lorcaserin Into Schedule VI, 78 FR 26701 (May 8, 2013); Placement of Lacosamide Into Schedule V, 74 FR 23789 (May 21, 2009); Rescheduling of the FDA Approved Product Containing Synthetic Dronabinol From Schedule II to Schedule III, 64 FR 35928 (July 2, 1999); Placement of Pemoline in Schedule IV, 40 FR 4150 (Jan. 28, 1975). Therefore, DEA has decided not to grant your request.

Sincerely,

**THOMAS
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Thomas W. Prevoznik
Assistant Administrator
Diversion Control Division



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Office of the Assistant Secretary for Health
Washington, D.C. 20201

August 29, 2023

The Honorable Anne Milgram
Administrator
Drug Enforcement Administration
U.S. Department of Justice
8701 Morrisette Drive
Springfield, VA 22152

Dear Anne Milgram:

Pursuant to the Controlled Substances Act (CSA), 21 U.S.C. 811(b) and (c), I, the Assistant Secretary for Health, am recommending that marijuana, referring to botanical cannabis (*Cannabis sativa L.*) that is within the definition "marihuana" or "marijuana" in the CSA, be controlled in Schedule III of the CSA.

Upon consideration of the eight factors determinative of control of a substance under 21 U.S.C. 811(c), the Food and Drug Administration (FDA) recommends that marijuana be placed in Schedule III of the CSA. The National Institute on Drug Abuse has reviewed the enclosed documents (which were prepared by FDA's Controlled Substance Staff and are the basis for FDA's recommendation) and concurs with FDA's recommendation. Marijuana meets the findings for control in Schedule III set forth in 21 U.S.C. 812(b)(3).

Based on my review of the evidence and FDA's recommendation, it is my recommendation as the Assistant Secretary for Health that marijuana should be placed in Schedule III of the CSA.

Should you have any questions regarding this recommendation, please contact FDA's Center for Drug Evaluation and Research, Office of Executive Programs (cderecsec@cder.fda.gov), at (301) 796-3200.

Sincerely,

A handwritten signature in black ink, appearing to read "RL Levine MD", is positioned above the typed name.

Rachel L. Levine, M.D.
ADM, USPHS
Assistant Secretary for Health

Enclosure

BASIS FOR THE RECOMMENDATION TO RESCHEDULE MARIJUANA INTO SCHEDULE III OF THE CONTROLLED SUBSTANCES ACT

I. Introduction

Background

On October 6, 2022, President Joseph R. Biden released a statement asking the Secretary of the Department of Health and Human Services (HHS) and the Attorney General “to initiate the administrative process to review expeditiously how marijuana is scheduled under federal law.”¹ This Presidential request led HHS to initiate a scientific and medical evaluation for botanical cannabis (*Cannabis sativa* L.) that is within the definition “marihuana” or “marijuana” in the federal Controlled Substances Act (CSA),² currently controlled under Schedule I of the CSA. As with prior evaluations conducted to reconsider the control status of marijuana under the CSA, the Food and Drug Administration (FDA) is conducting this evaluation and providing input and a scheduling recommendation to the Drug Enforcement Administration (DEA) in the form of an Eight Factor Analysis (8FA), pursuant to paragraphs (a) through (c) of section 201 and paragraph (b) of section 202 of the CSA (21 U.S.C. 811 (a-c) and 21 U.S.C. 812(b)).³

Since 2000, HHS (through the FDA and the National Institute on Drug Abuse (NIDA)) has conducted four scientific and medical evaluations of marijuana for drug scheduling purposes, in the form of 8FAs. (The process for developing an 8FA is elaborated below under *Considerations for Scheduling of Marijuana*.) The two most recent HHS 8FAs for marijuana were conducted in 2015 at the request of the DEA to enable them to respond to two petitions requesting removal of marijuana from Schedule I and placement in another schedule of the CSA. After reviewing the 8FAs conducted by HHS, DEA denied both petitions and maintained marijuana in Schedule I of the CSA.⁴

At the conclusion of an 8FA, three findings need to be made to determine the scheduling recommendation for a substance: its relative abuse potential compared to other drugs, whether it has a currently accepted medical use (CAMU) in treatment in the United States (or a currently

¹ Statement from President Biden on Marijuana Reform; <https://www.whitehouse.gov/briefing-room/statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform/>.

² Under 21 U.S.C. 802(16): “(16)(A) Subject to subparagraph (B), the terms “marihuana” and “marijuana” mean all parts of the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.

(B) The terms “marihuana” and “marijuana” do not include—

(i) hemp, as defined in section 1639o of title 7; or

(ii) the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom)

³ We acknowledge that the DEA, acting on behalf of the Attorney General, may ultimately implement any changes in the federal control status of marijuana pursuant to section 201(d)(1) of the CSA (21 U.S.C. 811(d)(1)), due to the control of cannabis and cannabis preparations internationally in Schedule I of the Single Convention on Narcotic Drugs of 1961 (hereafter, the Single Convention), and the requirement for the United States to be compliant with control measures stipulated for drugs controlled under the Single Convention.

⁴ Denial of Petition To Initiate Proceedings To Reschedule Marijuana, 81 FR 53688 (Aug. 12, 2016); Denial of Petition To Initiate Proceedings To Reschedule Marijuana, 81 FR 53767 (Aug. 12, 2016).

accepted medical use with severe restrictions (21 U.S.C. 812(b)(2)(B)), and its relative safety or ability to produce physical dependence compared to other drugs, as provided under 21 U.S.C. 812(b). After the Presidential request in October 2022, HHS (through FDA and NIDA) applied a two-part test to evaluate CAMU (hereinafter, “CAMU test”); this test takes into account the current widespread medical use of marijuana under the supervision of licensed health care practitioners (HCPs) under state-authorized programs.

Under Part 1 of the CAMU test, the Office of the Assistant Secretary for Health (OASH) considered whether there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented state-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these state jurisdictions. Part 2 of the CAMU test, performed by the FDA, evaluated whether there exists some credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied.

An important difference in the present scientific and medical evaluation relative to the HHS 8FAs for marijuana from 2015 is that Congress amended the definition of “marijuana” in the CSA in 2018. This action narrowed the scope of what is considered marijuana under the CSA by removing “hemp” and chemical derivatives of “hemp”, as discussed below. When the CSA was enacted in 1970, the term “marijuana” covered all varieties of *Cannabis sativa* L., including chemovars and preparations with high concentrations of cannabinoid compounds with intoxicating effects, such as delta-9-tetrahydrocannabinol (Δ 9-THC), as well as chemovars and preparations with lower concentrations of Δ 9-THC and other cannabinoid compounds, which could include “industrial hemp.” Specifically, the 1970 definition of “marihuana” under section 102(16) of the CSA (21 U.S.C. 802(16)) stated that:

The term ‘marihuana’ means all parts of the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

In December 2018, the Agriculture Improvement Act (also known as the 2018 Farm Bill), was signed into law, which defined “hemp” as “a plant species *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a total Δ 9-THC concentration of not more than 0.3 percent on a dry weight basis” (revising Section 297A of the Agricultural Marketing Act of 1946 (specifically, 7 U.S.C. 1639o). The 2018 Farm Bill explicitly removed “hemp” categorically from the definition of marijuana in the CSA, which removed it from control under any drug schedule of the CSA. Based on the provisions of the 2018 Farm Bill, the current definition of marijuana under 21 U.S.C. 802(16) is as follows:

(16)(A) Subject to subparagraph (B), the terms “marihuana” and “marijuana” mean all parts of the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin

extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.

(B) The terms “marihuana” and “marijuana” do not include—

- (i) hemp, as defined in section 1639o of title 7; or
- (ii) the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

In implementing the hemp provisions from the 2018 Farm Bill, DEA clarified that the definition of “Tetrahydrocannabinols” under 21 CFR 1308.11(d)(31) does not include “any material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.”⁵

The 2018 Farm Bill additionally had the effect of decontrolling many products containing predominantly cannabidiol (CBD) derived from hemp and containing no more than 0.3 percent Δ^9 -THC on a dry weight basis. This included the FDA-approved product Epidiolex, which contains plant-derived, highly purified CBD as its active ingredient and was approved by FDA in June 2018, just prior to the enactment of the Farm Bill. Prior to FDA approval of Epidiolex, CBD was a Schedule I substance, based on its derivation from marijuana. To address the Epidiolex approval, DEA placed “approved cannabidiol drugs” into Schedule V of the CSA in September 2018, under 21 CFR 1308.15(f),⁶ and asserted that the placement was necessary to carry out United States obligations under the Single Convention. Notably, though, FDA’s review of the NDA for Epidiolex, as well as the subsequent HHS 8FA, found that, “Based on the totality of the available scientific data, CBD does not have meaningful abuse potential. In support of this finding, the evidence for any abuse potential is also substantially less than that of all substances currently in Schedule V.” Thus, the decontrol of FDA-approved drugs that contain CBD derived from cannabis with no more than 0.1 percent Δ^9 -THC on a dry weight basis is scientifically supported by preclinical and clinical study data. Products containing predominantly plant-derived CBD or marketed with the intent of offering consumers a plant-derived, CBD-containing product, will not be addressed in this scientific and medical evaluation of marijuana. It should be noted some hemp-derived CBD products may contain Δ^9 -THC or other cannabinoids in amounts sufficient to produce drug effects more associated with marijuana, and may or may not be legally within the definition of marijuana. It is acknowledged that their widespread use may contribute to the epidemiological data on marijuana use that is discussed in Factors 4, 5, and 6 of this scientific and medical evaluation.

It is important to note that, to date, FDA has not approved an NDA for a drug product containing botanical marijuana. However, two drug products containing Δ^9 -THC (as dronabinol, which is specifically the (-)-*trans*- Δ^9 -THC stereoisomer), the primary compound in marijuana that is

⁵ 85 FR 51639, 51639-51645, August 21, 2020

⁶ Under 21 CFR 1308.15(f): “Approved cannabidiol drugs. (1) A drug product in finished dosage formulation that has been approved by the United States Food and Drug Administration that contains cannabidiol (2-[1R-3-methyl-6R-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl-1,3-benzenediol) derived from cannabis and no more than 0.1 percent (w/w) residual tetrahydrocannabinols.”

responsible for its abuse potential, have received FDA approval: Marinol and Syndros. Dronabinol is a Schedule I substance under the CSA unless it is contained in an FDA-approved drug product, as described below.

Marinol (dronabinol) capsules, 2.5, 5, and 10 mg, received FDA approval in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who failed to respond adequately to conventional anti-emetic treatments. In 1992, FDA approved an additional indication for the treatment of anorexia associated with weight loss in patients with acquired immunodeficiency syndrome (AIDS). Following the 1985 Marinol approval, DEA conducted a product-specific rescheduling in 1986 for “synthetic dronabinol in sesame oil and encapsulated in soft gelatin capsules,” moving it from Schedule I into Schedule II. In 1999, DEA rescheduled “synthetic dronabinol in sesame oil and encapsulated in soft gelatin capsules” again, from Schedule II into Schedule III, based on low numbers of reports of abuse of Marinol relative to marijuana.

Syndros (dronabinol) oral solution 5 mg/ml received FDA approval in 2016 for the same indications as those approved for Marinol: nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments and anorexia associated with weight loss in patients with AIDS. Following FDA approval, DEA conducted a product-specific rescheduling in 2017 for “FDA-approved products containing dronabinol in an oral solution” from Schedule I into Schedule II.

Considerations for Scheduling of Marijuana

In considering the scheduling of marijuana in response to President Biden’s request, the Secretary of HHS is required to consider in a scientific and medical evaluation eight factors determinative of control under the CSA, pursuant to 21 U.S.C. 811(b). The eight factors are the following:

1. Its actual or relative potential for abuse;
2. Scientific evidence of its pharmacological effect, if known;
3. The state of current scientific knowledge regarding the drug or other substance;
4. Its history and current pattern of abuse;
5. The scope, duration, and significance of abuse;
6. What, if any, risk there is to the public health;
7. Its psychic or physiological dependence liability; and
8. Whether the substance is an immediate precursor of a substance already controlled.

Following consideration of the eight factors, three findings need to be made to determine the schedule for a drug or substance under the CSA. The three required findings relate to a substance’s abuse potential, CAMU in the United States, and safety or dependence potential (21 U.S.C. 812(b)).

In this document, the term “marijuana” will be used to refer to *Cannabis sativa L.*, to be responsive to language of the CSA definition of “marihuana” or “marijuana” and its listing as the Schedule I drug class that is subject of this evaluation. The present evaluation of marijuana discusses the scientific and medical information relative to each of the eight factors, presents

findings in the three required areas (abuse potential, CAMU, and safety or dependence liability) and makes a recommendation regarding the scheduling of marijuana.

It is important to note that this evaluation is necessarily limited in scope and depth to those preclinical, clinical, and epidemiological data that are directly related to determining the abuse potential, physical dependence, and CAMU of marijuana in response to the eight factors described in the CSA. As such, this assessment is comprehensive, but is not exhaustive or encyclopedic. Extensive reviews of marijuana and cannabinoids are publicly available in papers published in the scientific and medical literature, as well as from federal entities such as NIDA and the Congressional Research Service, from professional medical associations, and from the National Academies of Science, Engineering and Medicine (NASEM). The current review is largely focused on modern scientific considerations on whether marijuana has a CAMU and on new epidemiological data related to abuse of marijuana in the years since the 2015 HHS 8FAs on marijuana.

In the epidemiological analyses below regarding prevalence of marijuana abuse and associated harms, evaluations included comparators such as heroin (Schedule I), fentanyl (Schedule II), oxycodone (Schedule II), hydrocodone (Schedule II), cocaine (Schedule II), ketamine (Schedule III), benzodiazepines (Schedule IV), zolpidem (Schedule IV), tramadol (Schedule IV), and alcohol (FDA Office of Surveillance and Epidemiology, 2023). Each individual epidemiological database evaluated a specific group of drugs and not every comparator was evaluated under each database.

It should be noted that although alcohol is well known to be abused, it was explicitly exempted from control under the CSA when it was enacted. Typically, substances that are not controlled under the CSA are not utilized as comparator drugs for scheduling placement considerations because they may not have been formally evaluated for abuse potential in standard preclinical and clinical abuse-related studies. However, alcohol is included in the analyses because of its extensive availability and use in the United States, which is also observed for nonmedical use of marijuana (also known as recreational use of marijuana).

After assessing all available preclinical, clinical, and epidemiological data, FDA recommends that marijuana be rescheduled from Schedule I into Schedule III of the CSA. Schedule III drugs are classified as having a potential for abuse less than the drugs or other substances in schedules I and II, a currently accepted medical use in treatment in the United States, and moderate or low physical dependence or high psychological dependence that may result from their use. NIDA concurs with this recommendation.

II. Evaluating Marijuana Under the Eight Factors

Pursuant to 21 U.S.C. 811(c), the eight factors pertaining to the scheduling of marijuana are considered below.

FACTOR 1. ITS ACTUAL OR RELATIVE POTENTIAL FOR ABUSE

Under the first factor, the Secretary must consider actual or relative potential for abuse of marijuana. The CSA does not define the term “abuse.” However, the CSA’s legislative history suggests using the following criteria in determining whether a particular drug or substance has a potential for abuse⁷:

- a. There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.
- b. There is a significant diversion of the drug or drugs containing such a substance from legitimate drug channels.
- c. Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice.
- d. The drug or drugs containing such a substance so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

In the development of this scientific and medical evaluation for the purpose of scheduling, the Secretary analyzed considerable data related to the abuse potential of marijuana. Determining the abuse potential of a substance is complex with many dimensions, and no single test or assessment provides a complete characterization. Thus, no single measure of abuse potential is ideal. Scientifically, a comprehensive evaluation of the relative abuse potential of a substance can include consideration of the following elements: chemistry, receptor binding, behavioral effects indicating that the substance is rewarding or is similar to another substance controlled under the CSA, pharmacokinetics, behavioral effects indicating that the substance produces physical or psychic dependence, and epidemiological data related to abuse of the substance regarding its pattern and duration of use, as well as the risk it presents to the public health.

- a. **There is evidence that individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.**

Evidence shows that some individuals are taking marijuana in amounts sufficient to create a hazard to their health and to the safety of other individuals and the community. However,

⁷ Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970) reprinted in U.S.C.A.N. 4566, 4603.

evidence also exists showing that the vast majority of individuals who use marijuana are doing so in a manner that does not lead to dangerous outcomes to themselves or others.

The data supportive of this conclusion are found in Factor 4 (below), “Its History and Current Pattern of Abuse” (citing data from National Survey on Drug Use and Health (NSDUH), the Behavioral Risk Factor Surveillance System (BRFSS), the Research Abuse, Diversion and Addiction-Related Surveillance (RADARS) System’s Nonmedical Use of Prescription Drugs (NMURx) Program, Monitoring the Future (MTF), the Youth Risk Behavior Surveillance System (YRBSS), and the International Cannabis Policy Survey (ICPS)), in Factor 5, “The Scope, Duration, and Significance of Abuse” (citing data from National Poison Data System (NPDS), NSDUH, the Treatment Episode Data Set (TEDS), National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO), the Nationwide Emergency Department Sample (NEDS), and the National Inpatient Sample (NIS)), and Factor 6, “What, if any, Risk There is to the Public Health” (citing data from NSDUH, TEDS, NEDS, NIS, ToxIC Core Registry, FDA Adverse Event Reporting System (FAERS), FDA’s Center for Food Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (CAERS), National Vital Statistics System-Mortality and Drug-Involved Mortality (NVSS-M and DIM), the Drug Abuse Warning Network (DAWN), FDA’s Sentinel Distributed Database System, and Centers for Medicare and Medicaid Services (CMS)).

To provide context, from 2015 to 2019, the prevalence of past-year use of alcohol was 5-6 times greater than that of past-year nonmedical use of marijuana. In contrast, the prevalence of past-year nonmedical use of heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem was 4-5 times less than that for marijuana.

In NSDUH, among people with past-year marijuana nonmedical use, approximately half of individuals reported nonmedical marijuana use an average of less than 5 days/month while another 30% reported nonmedical marijuana use for an average of more than 20 days/month. In the BRFSS population of people with past-30-day marijuana use, near-daily use was more likely if the individual was using marijuana for medical reasons. However, medical-only use of marijuana was less common (25% for medical-only use, compared to 39% for medical and nonmedical use, and 36% for nonmedical use only). Additionally, in NSDUH, past-year use of marijuana was predictive of past-month use for 60-80% of respondents, similar to alcohol use (approximately 80% of those who used alcohol in the past year also did so in the past month).

The most notable conclusion from an evaluation of various epidemiological databases of adverse outcomes involving marijuana or comparator drugs that are used nonmedically, occurring over 2015 to 2021, is that the utilization-adjusted rate of adverse outcomes involving marijuana was consistently lower than the respective utilization-adjusted rates of adverse outcomes involving heroin, cocaine, and, for certain outcomes, other comparators. Also, the rank order of the comparators in terms of adverse outcome counts typically placed alcohol or heroin in the first or immediately subsequent positions, with marijuana in a lower place in that ranking. This pattern was also observed for serious medical outcomes, including death, observed in Poison Center data, where marijuana was in the lowest ranking group. This suggests consistency across databases, across drugs, and over time, and although abuse of marijuana produces clear evidence of harmful consequences, these appear to be relatively less common and less severe than some

other comparator drugs. Importantly, these comparisons of prevalence of adverse outcomes were from descriptive analyses only. Thus, underlying differences in the populations being compared (e.g., age or pre-existing medical conditions) may have contributed to observed differences in outcome frequency and severity, and the ranked order across comparators. In addition, because individuals using marijuana and/or the selected comparators may have been monitored differently, there may have been differences between the populations in outcome ascertainment.

The risks to the public health posed by marijuana are lower compared to other drugs of abuse (e.g., heroin, oxycodone, cocaine), based on an evaluation of various epidemiological databases for emergency department (ED) visits, hospitalizations, unintentional exposures, and most importantly, for overdose deaths. The rank order of the comparators in terms of greatest adverse consequences typically places heroin, benzodiazepines and/or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking, especially when a utilization adjustment is calculated. For overdose deaths, marijuana is always in the lowest ranking among comparator drugs. These evaluations demonstrate that there is consistency across databases, across substances, and over time that although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs.

b. There is significant diversion of the substance from legitimate drug channels.

There is a lack of evidence of significant diversion of marijuana from legitimate drug channels (i.e., marijuana that is legally marketed under United States federal law), due to the fact that an NDA for a drug product containing botanical marijuana has not been approved for marketing in the United States. Marijuana is used by researchers for clinical research under investigational new drug (IND) applications, and there are multiple DEA-registrants who have applied and are approved to produce marijuana and derived formulations for use in DEA-authorized nonclinical and clinical research. These research and manufacturing authorizations represent the only legitimate federally sanctioned drug channels in the United States, and there is a lack of data indicating diversion occurring from these entities or activities. However, there are significant additional sources of marijuana in the United States, both from illicit cultivation and production, illicit importation from other countries, and from state programs that permit dispensing of marijuana for medical use and, in some states, recreational adult use.

c. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances.

FDA has not approved an NDA for a drug product containing botanical marijuana for any therapeutic indication. Thus, at the federal level, the only way an individual can use marijuana on the basis of medical advice through legitimate channels under federal law is by participating in research under an IND. However, 38 states and the District of Columbia have passed state-level medical marijuana laws allowing for individuals to use marijuana under certain circumstances for medical purposes. Outside of the federal- and state-sanctioned medical use of marijuana, individuals are using marijuana on their own initiative for medical as well as nonmedical purposes. Epidemiological data related to nonmedical use of marijuana is detailed in Factor 4, “Its History and Current Pattern of Abuse.”

- d. The substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.**

Marijuana has been a Schedule I substance under the CSA since it was enacted in 1970. The primary compound in marijuana that is responsible for its abuse potential is Δ 9-THC (also known as dronabinol, when specifically referring to the (-)-*trans*- Δ 9-THC stereoisomer), which has agonist activity at cannabinoid CB₁ receptors. As discussed under Factor 2, there are extensive nonclinical and clinical studies that establish that marijuana, due to the CB₁ agonist activity of its main cannabinoid constituent Δ 9-THC, produces rewarding effects that would be consistent with observed long-term patterns of nonmedical use and abuse, both before and in years since enactment of the CSA (see Factor 4). Additionally, FDA has approved two drug products containing dronabinol: Marinol (in 1985; Schedule III) and Syndros (in 2016; Schedule II). When these products were being developed, they underwent a systematic evaluation of their abuse potential based on animal and human behavioral studies, which showed that dronabinol has abuse potential. The abuse-related studies for Marinol and Syndros confirmed the abuse potential of Δ 9-THC, the primary compound responsible for the abuse of marijuana. These findings suggest that marijuana will continue to be used nonmedically, diverted from legitimate channels, and trafficked in illicit channels as a potential source for continued nonmedical use in the United States (see Factor 5).

Epidemiological data indicate that marijuana has the potential for creating hazards to the health of the user and to the safety of the community. However, as a relative finding on abuse liability, when comparing marijuana to heroin, oxycodone, hydrocodone, fentanyl, cocaine, ketamine, benzodiazepines, zolpidem, tramadol, and alcohol in various epidemiological databases that allow for some or all of these comparisons, marijuana is not typically among the substances producing the most frequent incidence of adverse outcomes or severity of substance use disorder (see Factors 4, 5, and 6). However, as noted above in Factor 1a, there are limitations in comparing descriptive data on adverse outcomes across drugs.

FACTOR 2. SCIENTIFIC EVIDENCE OF ITS PHARMACOLOGICAL EFFECTS, IF KNOWN.

Under the second factor, the Secretary must consider the scientific evidence of the pharmacological effects of marijuana, based on the effects of Δ 9-THC, the primary compound responsible for the abuse potential of marijuana. This section includes a scientific evaluation of the neurochemistry, receptor pharmacology, animal abuse-related behavioral effects, and human behavioral and physiological effects of marijuana. The overview presented below relies upon the current scientific information available in the public domain.

Neurochemistry and Receptor Pharmacology of Marijuana

Cannabis is the genus of a plant that contains numerous natural constituents, including cannabinoids (see Factor 3, below). Marijuana samples derived from various cultivated chemovars may vary with respect to their composition and concentration of various chemical constituents, including whether they contain significant amounts of Δ^9 -THC or other cannabinoids (Appendino et al., 2011; Smith et al., 2022). As a consequence, marijuana products from different strains will have differing biological and pharmacological profiles.

Marijuana contains at least 560 identified natural constituents, including 125 compounds classified as cannabinoids (Appendino et al., 2011; Elsohly & Slade, 2005; Radwan et al., 2021). Most major cannabinoid compounds occurring naturally in *Cannabis* have been identified chemically, but new and minor compounds are continuously being characterized (Pollastro et al., 2011; Radwan et al., 2021). The chemistry of marijuana is described in more detail in Factor 3, “The State of Current Scientific Knowledge Regarding the Drug or Other Substance.”

The two most abundant cannabinoids present in marijuana are Δ^9 -THC and CBD (Lewis et al., 2018). Mechoulam and Gaoni first described the structure and function of Δ^9 -THC in 1965, while Mechoulam and Shvo first described the structure of CBD in 1963 (Mechoulam & Gaoni, 1965; Mechoulam & Shvo, 1963). Δ^9 -THC is the major psychoactive intoxicating cannabinoid in marijuana (Wachtel et al., 2002) and is the component of marijuana that is primarily responsible for its abuse potential. In contrast, CBD has negligible abuse potential, as assessed by FDA during the NDA review for Epidiolex, an FDA-approved drug product containing plant-derived, highly-purified CBD (Epidiolex drug label, 2022) .

There are two cannabinoid receptors: CB₁ and CB₂. The identification and cloning of CB₁ receptors from rat brain tissue (Devane et al., 1988) and then from human brain tissue (Gerard et al., 1991) was followed by identification and cloning of CB₂ receptors in the periphery (Munro et al., 1993) .

CB₁ and CB₂ receptors belong to the family of G-protein-coupled receptors and present a typical seven transmembrane-spanning domain structure. Cannabinoid receptors primarily link to an inhibitory G-protein (G_{i/o}), such that adenylate cyclase activity is inhibited when a cannabinoid ligand binds to the receptor. This, in turn, prevents the conversion of adenosine triphosphate (ATP) to the second messenger, cyclic AMP (cAMP), which decreases cAMP levels (Eldeeb et al., 2020; Howlett et al., 2004). Kesner et al. (Kesner & Lovinger, 2021) have summarized the second messenger functioning in more depth, noting that G proteins also contain beta/gamma G protein units that are also liberated following ligand binding, which then bind to and alter ion channel function, including inhibition of voltage-gated ion channels and activation of potassium channels. Ligand binding can also activate some subforms of phospholipase C as well as beta-arrestin protein. All of these second messenger routes amplify the neural signal following cannabinoid binding at CB₁ and CB₂ receptors.

CB₁ receptors are found primarily in the central nervous system (CNS), but are also present in peripheral tissues, such as liver, heart, and lungs (Howlett & Abood, 2017). In the brain, CB₁ receptors are expressed with highest density in cortical regions, hippocampus, basal ganglia, and

cerebellum (Herkenham et al., 1991; Howlett et al., 2004; Marsicano & Kuner, 2008) and lowest density in brainstem and hypothalamic areas (Howlett et al., 2004; Busquets-Garcia et al., 2018). The localization of these receptors may explain cannabinoid effects on movement coordination, memory, and cognition. Additionally, CB₁ receptors are found in glial cells (Breivogel & Sim-Selley, 2009) as well as in the immune system (Klein et al., 2003). However, the concentration of CB₁ receptors is considerably lower in peripheral tissues than in the CNS (Herkenham, 1992; Herkenham et al., 1990).

CB₂ receptors are found primarily in the immune system (Klein et al., 2003; Mackie & Stella, 2006), including numerous leukocyte cell types (Bouaboula et al., 1993; Turcotte et al., 2016), as well as in activated CNS microglia (Mackie, 2008). Additionally, CB₂ receptors have been localized in the brain, primarily in the cerebellum and hippocampus (Gong et al., 2006). The distribution of CB₂ receptors throughout the body is less extensive than the distribution of CB₁ receptors (De Petrocellis & Di Marzo, 2009).

There are two endogenous cannabinoid receptor agonists, anandamide (identified in 1992) and arachidonyl glycerol (2-AG; identified in 1995) (Di Marzo, 2006). At CB₁ receptors, anandamide is a partial agonist with low intrinsic efficacy (Mackie, 2008) while 2-AG is a full agonist with high intrinsic efficacy (Gonsiorek et al., 2000). These endogenous cannabinoid ligands are present in central as well as peripheral tissues. A combination of uptake and hydrolysis terminate the action of anandamide and 2-AG. The endogenous cannabinoid system is a locally active signaling system, activated “on demand” in response to changes to the local conditions to help restore homeostasis (Medeiros et al., 2020). The endogenous cannabinoid system, including the endogenous cannabinoids and the cannabinoid receptors, demonstrate substantial plasticity in response to several physiological and pathological stimuli (Augustin & Lovinger, 2018; De Petrocellis & Di Marzo, 2009). This plasticity is particularly evident in the CNS.

Δ9-THC and CBD have varying affinity and effects at the cannabinoid receptors. Δ9-THC is a partial agonist at both CB₁ (K_i = 18-218 nM) and CB₂ receptors (K_i = 36-309 nM) (Tagen and Klumpers, 2022). However, CB₁ receptors are the main pharmacological site of action for Δ9-THC, making CB₁ receptors the site that is responsible for the abuse potential of marijuana (Zimmer et al., 1999). The other CNS site where Δ9-THC may have activity is the 5HT₃ receptor, where it functions as an antagonist (Barann et al., 2002; Shi et al., 2012). In contrast, CBD has low affinity for both CB₁ and CB₂ receptors (McPartland et al., 2007; Mechoulam et al., 2007) and may act as a negative allosteric modulator and/or weak antagonist at these sites (Morales et al., 2017; Thomas et al., 2007). CBD has additional CNS effects as a serotonin 5HT_{1A} agonist and a serotonin 5HT_{2A} weak partial agonist (Russo et al., 2005), and well as a serotonin 5HT_{3A} antagonist (Yang et al., 2010).

In the past 30 years, the potency of marijuana with regard to Δ9-THC has increased dramatically. As reported in 2021 by ElSohly et al., the concentration Δ9-THC in marijuana samples in the United States increased from 3% in 1991 to 4.47% in 1997, from 3.4% in 1993 to 8.8% in 2008, from 4% in 1995 to 12% in 2014, and from 8.9% in 2008 to 17.1% in 2017. These increases were attributed by ElSohly et al. to an increase in the number of high potency samples (i.e., sinsemilla) in the overall samples tested. In contrast, there was a decrease initially in the

concentration of CBD in the same samples, from 0.40% in 2009 to 0.14% in 2017, but this rose to 0.60% in 2019. Based on an evaluation of marijuana seized by DEA, the majority of samples contained high concentrations of Δ 9-THC and low concentrations of CBD (ElSohly et al., 2021).

Animal Abuse-Related Behavioral Effects

Self-Administration

Self-administration is a method that assesses the ability of a drug to produce rewarding effects. The presence of rewarding effects increases the likelihood of behavioral responses to obtain additional drug. Animal self-administration of a drug is often useful in suggesting whether humans will experience that a particular substance will have rewarding effects, which is indicative of abuse potential. A good correlation is often observed between those drugs that rhesus monkeys self-administer and those drugs that humans abuse (Balster & Bigelow, 2003).

Since self-administration is a methodology in which the test drug is typically administered intravenously to rats, it is not possible to evaluate botanical marijuana through self-administration. However, given that Δ 9-THC is the primary substance that confers abuse potential to marijuana, its ability to induce self-administration can serve as an indicator of the abuse potential of marijuana.

For many decades, researchers had difficulty producing consistent self-administration of Δ 9-THC in animals (Harris et al., 1974; Kaymakcalan, 1973; Mansbach et al., 1994; Pickens et al., 1973; van Ree et al., 1978). When novel training paradigms were developed, intravenous self-administration of Δ 9-THC was eventually established in a variety of animal models (Braidia et al., 2004; Justinova et al., 2005; Justinova et al., 2004; Justinova et al., 2003; Tanda et al., 2000).

In the past 20 years, investigators have continued to experiment with Δ 9-THC self-administration in animal investigations by varying the methodology, testing differences in animal species and sex, route of administration (intravenous, oral, or inhalation of vaporized or combusted Δ 9-THC), dose of Δ 9-THC, and the schedule of reinforcement (fixed ratio and/or fixed interval). Based on the specific methods used, laboratories have had variable success in producing self-administration of Δ 9-THC.

Some studies showed successful animal self-administration of Δ 9-THC following intravenous administration (John et al., 2017; Justinova et al., 2003; Spencer et al., 2018; Stringfield & Torregrossa, 2021) administration of inhaled vapor (Freels et al., 2020), oral administration (Abraham et al., 2020; Nelson et al., 2019; Smoker, Hernandez, et al., 2019; Smoker, Mackie, et al., 2019), and intracerebroventricular administration (Braidia et al., 2001; Zangen et al., 2006). The repeated self-administration in these studies show that Δ 9-THC produces rewarding effects that lead an animal to repeatedly seek out the substance, which demonstrates that Δ 9-THC is reinforcing.

In contrast, there are other recent animal studies that have not been able to produce Δ 9-THC self-administration following intravenous administration (Lefever et al., 2014; Wakeford et al., 2017) and oral administration (Barrus et al., 2018). However, these negative data demonstrate how the

specific methodology used in a study can limit a behavioral response, and thus do not negate the positive results from the studies in which $\Delta 9$ -THC was actively self-administered by animals.

Typically, animal self-administration is used primarily to predict whether a novel substance is likely to be used by humans for its rewarding properties, as an indication of its abuse potential. However, it is well-known from epidemiological data that humans self-administer substances that contain $\Delta 9$ -THC, including botanical marijuana (see Factors 4, 5, and 6), for their ability to produce positive subjective responses, including euphoria. Thus, a comprehensive deconstruction of which animal methodology is optimum for producing preclinical self-administration of $\Delta 9$ -THC is not necessary for an evaluation of the abuse potential of marijuana in humans, since it is already clear that humans utilize marijuana for its rewarding properties.

Conditioned Place Preference

Conditioned place preference (CPP) is a less rigorous method than self-administration of determining whether drugs have rewarding properties. In this behavioral test, animals are given the opportunity to spend time in two distinct environments: one where they previously received a drug and one where they received a placebo. If the drug has rewarding properties, animals will choose to spend more time in the environment paired with the drug than the one paired with the placebo, when both options are presented simultaneously.

Many attempts to produce animal CPP with $\Delta 9$ -THC were unsuccessful, producing either no CPP (Parker & Gillies, 1995; Vlachou et al., 2007) or a conditioned place aversion (where an animal avoids the side of the cage where the drug was given, suggesting the drug was experienced as unpleasant) (Cheer et al., 2000; Hutcheson et al., 1998; Quinn et al., 2008; Sanudo-Pena et al., 1997; Schramm-Sapota et al., 2007). This is similar to the experimental difficulties reported in producing animal self-administration of $\Delta 9$ -THC.

In 1995, CPP was first shown to be elicited from exposure to $\Delta 9$ -THC (Lepore et al., 1995), followed by success by other investigators in producing CPP associated with $\Delta 9$ -THC (Braida et al., 2004; Castane et al., 2003; Ghosland et al., 2002; Le Foll et al., 2006; Soria et al., 2004; Valjent & Maldonado, 2000; Valjent et al., 2002).

The studies in which $\Delta 9$ -THC successfully produced CPP occurred under very specific experimental conditions, similar to the $\Delta 9$ -THC self-administration studies in animals. Experimental manipulations in CPP studies with $\Delta 9$ -THC have included varying animal species, sex, dose, route of administration, introduction of flavors to obscure unpleasant taste, and the drug history of the animals tested. However, as with animal self-administration, the use of CPP is typically to determine if a new drug produces rewarding sensations, which would suggest that a drug has abuse potential. Since it is clear that humans self-administer substances that contain $\Delta 9$ -THC, including botanical marijuana, it is not necessary to interrogate which CPP methods are optimal for demonstrating that $\Delta 9$ -THC has rewarding properties in animals.

Drug Discrimination Studies

Drug discrimination is a method in which animals indicate whether a test drug produces sensations similar to those produced by a training drug with a known pharmacological mechanism of action. In this test, an animal learns to press one bar in a test cage when it receives the training drug and another bar when it receives placebo. A challenge session with the test drug determines which of the two bars the animal presses more often, as an indicator of whether the test drug produces effects that are similar to the training drug. Drug discrimination is only considered to be an abuse-related study when the training drug is a known drug of abuse that is scheduled under the CSA and the test drug may have abusable effects similar to the training drug, based on having a similar mechanism of action to the training drug.

Δ^9 -THC, the primary compound in marijuana that is responsible for its abuse potential, is used extensively as the training drug in animal drug discrimination studies to demonstrate whether a novel compound produces cannabinoid effects. Since Δ^9 -THC is already considered to be the standard for establishing if new drugs have classic marijuana-like pharmacological activity in drug discrimination, the application of this method in evaluating the abuse potential of Δ^9 -THC will not be discussed further.

Human Behavioral and Physiological Effects

Subjective Effects of Δ^9 -THC

The psychological, behavioral, and subjective responses to marijuana in humans have been known and characterized since antiquity (Chaachouay et al., 2023; Russo, 2016). In the modern period, data on the psychological, behavioral, and subjective responses to marijuana are available from the drug label of FDA-approved drug products, from prospective human abuse potential (HAP) studies, from accounts published in the scientific and medical literature, and from an evaluation published in 2017 by the NASEM.

FDA-Approved Drug Products Containing Δ^9 -THC

Clinical scientific studies have investigated the effects of Δ^9 -THC, the primary compound responsible for the abuse potential of marijuana, on humans during the drug development of the FDA-approved drug product Marinol, which contains 2.5, 5, and 10 mg dronabinol ((-)-trans- Δ^9 -THC of synthetic origin in sesame seed oil). Section 6.1 (Clinical Trials Experience) of drug labels for Marinol and Syndros (which relied on the safety data from Marinol during drug development) lists the following AEs as occurring in controlled clinical studies during drug development.

Incidence > 1%:

- **CNS:** amnesia, anxiety/nervousness, ataxia, confusion, depersonalization, hallucination
- **General:** asthenia
- **Cardiovascular:** palpitations, tachycardia, vasodilation/facial flush

Incidence 3% to 10%

- *CNS:* euphoria, paranoid reaction, somnolence, thinking abnormal, dizziness
- *Gastrointestinal:* Abdominal pain, nausea, vomiting

Human Abuse Potential Studies

HAP studies evaluate whether a test drug produces positive subjective responses, compared to placebo and a known drug of abuse that is scheduled under the CSA that serves as the positive control. If the test drug produces rewarding effects that are statistically significantly greater than placebo, and beyond the acceptable placebo range of response, it is an indication that the drug may have abuse potential. The relative abuse potential is suggested by the responses from the positive control on these measures, in comparison to the test drug.

For many decades, HAP studies have been conducted with marijuana and Δ 9-THC in subjects who had nonmedical experience with cannabinoids (Fogel et al., 2017; Hunault et al., 2014; Karschner et al., 2011; Kaufmann et al., 2010; Ramesh et al., 2013; Ranganathan et al., 2012; Schindler et al., 2020; Spindle et al., 2021; Wachtel & de Wit, 2000; Wachtel et al., 2002). In these studies, doses of Δ 9-THC ranging from 1.79 to 69 mg were administered to subjects using marijuana and/or isolated Δ 9-THC. Most of these studies used smoking or oral administration, with some studies using the intravenous route of administration.

There were commonalities in results among all of these HAP studies, despite the differences in dose of Δ 9-THC, the route of administration, or whether the Δ 9-THC was provided in the form of marijuana or isolated compound. Following administration of the study drug, there were increases on such positive subjective responses as visual analog scales (VAS) for Drug Liking, Overall Drug Liking, Good or Pleasant Drug Effects, High, Stoned, Stimulated, Enjoyment, Take Drug Again, Want More Drug, and Willing to Pay. There were also increases on the Addiction Research Center Inventory (ARCI) scales for Morphine Benzodrine Group (euphoria), Marijuana, and Amphetamine. These data consistently demonstrate that Δ 9-THC, in the form of marijuana or isolated compound, when administered under controlled experimental conditions, produces rewarding effects that are indicative of abuse potential.

Following administration of marijuana or Δ 9-THC, there were also increases on subjective responses assessing various negative drug effects and sedation, often delayed in onset from when the positive subjective effects began. These assessments included VAS for Bad Drug Effect, Sick, Dizzy, Hungry, Suspicious, Paranoid, Anxious, Sedated, Calm, Drowsy, Tired, Forgetful, Impaired Memory, Dry Mouth, and Dry/Red Eyes, as well as ARCI scales for Lysergic Acid Diethylamide (dysphoria), Benzodrine Group (stimulant), and Pentobarbital-Chlorpromazine-Alcohol Group (sedation).

Given the wide range of doses tested in HAP studies, these positive and negative subjective responses following administration of marijuana or Δ 9-THC were often dose-dependent. There were typically few differences between the responses between marijuana and Δ 9-THC, or between responses based on route of administration of the study drug.

Common Responses to Marijuana in Humans

The responses to dronabinol reported during drug development and in HAP studies parallel the common responses to marijuana that have been described by other medical scientists (Adams & Martin, 1996; Agrawal et al., 2014; American Psychiatric Association, 2013; Earleywine, 2002; Hollister, 1986, 1988), which include:

Positive Subjective Responses

- Euphoria
- Pleasurable “rush” or “buzz”
- Merriment
- Happiness
- Exhilaration

Sedative Responses

- Sedation
- Drowsiness
- Relaxation
- Changes in sleep

Anxiety and Negative Responses

- Anxiety
- Panic attack
- Fearfulness
- Agitation
- Paranoia
- Restlessness
- Dysphoria

Perceptual Changes

- Hallucinations
- Feelings seem stronger
- Sexual enhancement
- Spiritual enhancement
- Changes in time perception
- Changes in perception (sight, sound, taste, smell, touch)

Psychiatric, Social, and Cognitive Changes

- Drug abuse
- Illusions
- Delusions
- Depersonalization
- Heightened imagination
- Disinhibition
- Emotional lability

- Memory and concentration impairment
- Disorganized thinking
- Impaired judgment
- Confusion
- Increased sociability
- Talkativeness

Physiological Responses

- Nausea
- Tachycardia
- Facial flushing
- Dry mouth
- Tremor
- Dizziness
- Increased appetite, especially for sweet and fatty foods
- Reduced coordination
- Ataxia
- Hyperemesis

The positive changes that occur following use of marijuana are pleasurable to many humans and are associated with drug-seeking and drug-taking. These effects are typically dose-dependent, with higher doses and routes of administration that produce faster onset producing more intense responses and the likelihood of more negative subjective effects (Kesner & Lovinger, 2021).

National Academies of Science, Engineering, and Medicine

In 2017, NASEM published a book-length evaluation entitled *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research* (National Academies of Sciences & Medicine, 2017). In this evaluation, NASEM provided a brief summary of the clinical features of marijuana intoxication, as follows:

During acute cannabis intoxication, the user's sociability and sensitivity to certain stimuli (e.g., colors, music) may be enhanced, the perception of time is altered, and the appetite for sweet and fatty foods is heightened. Some users report feeling relaxed or experiencing a pleasurable "rush" or "buzz" after smoking cannabis (Agrawal et al., 2014). These subjective effects are often associated with decreased short-term memory, dry mouth, and impaired perception and motor skills. When very high blood levels of Δ^9 -THC are attained, the person may experience panic attacks, paranoid thoughts, and hallucinations [...] Furthermore, as legalized medical and nonmedical cannabis availability increase nationwide, the impairment of driving abilities during acute intoxication has become a public safety issue.

In addition to Δ^9 -THC dosage, two main factors influence the intensity and duration of acute intoxication: individual differences in the rate of absorption and metabolism of Δ^9 -THC, and the loss of sensitivity to its pharmacological actions. Prolonged CB₁ receptor

occupation as a consequence of the sustained use of cannabis can trigger a process of desensitization, rendering subjects tolerant to the central and peripheral effects of Δ^9 -THC and other cannabinoid agonists (Gonzalez et al., 2005). Animals exposed repeatedly to Δ^9 -THC display decreased CB₁ receptor levels as well as impaired coupling between CB₁ and its transducing G-proteins (Gonzalez et al., 2005). Similarly, in humans, imaging studies have shown that chronic cannabis use leads to a down-regulation of CB₁ receptors in the cortical regions of the brain and that this effect can be reversed by abstinence (Hirvonen et al., 2012).

In conclusion, Δ^9 -THC, the substance largely responsible for the abuse potential of marijuana, is an agonist at the cannabinoid CB₁ receptor. When Δ^9 -THC is administered to animals, it produces rewarding responses, as evidenced by its ability to induce self-administration and conditioned place preference. This is consistent with the data from human studies and from clinical observations, where administration of Δ^9 -THC or use of marijuana produces euphoria and other pleasurable responses, as well as sedation and anxiety responses. Psychiatric, social, and cognitive responses, which are often experienced as negative, are also reported, as are physiological responses such as dry mouth, ataxia, and increased hunger. As described in Factor 4, the rewarding responses observed in humans are consistent with the prevalence of nonmedical use of marijuana, which includes abuse of the substance. Abuse of marijuana by individuals can lead to other negative consequences, including addiction and the need to seek medical attention through calls to poison centers or visits to an ED, as described in Factor 5.

FACTOR 3. THE STATE OF CURRENT SCIENTIFIC KNOWLEDGE REGARDING THE DRUG OR OTHER SUBSTANCE

Under the third factor, the Secretary must consider the state of current scientific knowledge regarding marijuana. Thus, this section discusses the chemistry and human pharmacokinetics of marijuana, as well as whether marijuana has a CAMU in the United States.

Chemistry

Cannabis is a genus of annual flowering plant with digitate leaves in the family *Cannabaceae* Martinov (United States Department of Agriculture Natural Resources Conservation Service, 2023; WorldFloraOnline, 2023). Many scholars have studied diverse datasets and models to estimate the origins of *Cannabis*. It likely originated in Central or Southeast Asia over 10,000 years ago and was first cultivated in China for fiber and seed production (Bonini et al., 2018; Russo et al., 2008), with cultivation spreading across Asia, Africa, and Europe and eventually to the Americas (Pisanti & Bifulco, 2019). A long-standing and significant historical debate by botanists and taxonomists continues today regarding the number of species in the *Cannabis* genus (Clarke & Watson, 2007; Hillig, 2005; Russo, 2004; Schultes et al., 1974; Small & Cronquist, 1976). It is generally treated as a single, highly polymorphic species known as *Cannabis sativa* L., with the other two previously reported species listed as *Cannabis indica* Lam. and *Cannabis ruderalis* Janisch (United States Department of Agriculture Agricultural Research Service, 2023). Plants previously believed part of the latter two species are generally recognized as varieties (or subspecies) of *Cannabis sativa* L. (*C. sativa*), which are commonly

referred to as var. *indica* and var. *ruderalis*. *Cannabis sativa* and var. *indica* plants are widely cultivated for their size, branching, and cannabinoid content, while *ruderalis* is rarely cultivated alone as it is shorter, often unbranched, and has very low cannabinoid content (Thomas & ElSohly, 2016a). Worldwide *Cannabis* varieties are separated into hundreds of different cultivars and strains. Plants selected for cultivation are known as cultivated varieties or cultivars, whereas plants reproduced asexually from a cultivar through clonal propagation are known as strains (Procaccia et al., 2022). These practices have resulted in significantly different chemical profiles for *Cannabis* cultivars and the classification term to account for these chemical profile differences has evolved. The term ‘chemovar’ accounts for the plant’s chemical profile and is a more meaningful classification for clinical researchers studying the plant’s potential drug effects (Hazekamp & Fisdick, 2012).

Cannabis is a dioecious plant (WorldFloraOnline, 2023), meaning female and male flowers occur on separate plants, and rarely occurs as a monoecious plant (single plant containing male and female flowers). The glandular trichomes found on the female plant’s unfertilized flower heads and bracts contain the highest concentrations of cannabinoids. For this reason, unfertilized female chemovars are favored to harvest large inflorescences (i.e., complete flower head) for their rich cannabinoid and terpene content. ^{Error! Bookmark not defined.} Consequently, marijuana products developed from diverse chemovars will have different safety, biological, pharmacological, and toxicological profiles.

The *C. sativa* plant naturally contains many different compounds and more than 550 have been identified, such as: cannabinoids, terpenoids, flavonoids, stilbenoids, steroids, polysaccharides, benzoquinone, phenanthrenes, spiroindans, lignans, fatty acids, sugars, hydrocarbons, amino acids, and proteins (Liu et al., 2022; Rock & Parker, 2021). Cannabinoids are mainly found in living *C. sativa* plants in their non-psychoactive carboxylated forms (i.e., acid form), which require drying, heating, combustion, or aging to decarboxylate to their neutral forms, (Thomas & ElSohly, 2016b) and are primarily composed of C₂₁ terpenophenolic compounds (Brenneisen, 2007). The most abundant neutral form cannabinoids are Δ^9 -THC and CBD, but nearly 200 have been identified (ElSohly et al., 2017; Johnson et al., 2020) in the plant and are divided into subclasses: cannabigerols (CBGs), cannabichromenes (CBCs), cannabidiols (CBDs), (-)- Δ^9 -trans-tetrahydrocannabinols (Δ^9 -THCs), (-)- Δ^8 -trans-tetrahydrocannabinols (Δ^8 -THCs), cannabicyclols (CBLs), cannabielsoins (CBEs), cannabinols (CBNs), cannabinodiols (CBNDs), cannabitriols (CBTs), and the miscellaneous cannabinoids (Thomas & ElSohly, 2016a).

Like any other botanical substance, marijuana plants are heterogeneous in nature and contain a complex chemical profile. Moreover, variable organic plant material, as well as manufactured preparations, result in a variety of product forms that dictate different routes of administration, associated risks, and differences in quality of the product used, which may also influence risk for users. The potential for high variability of marijuana and marijuana-derived products, both in product composition and impurity profile, are major considerations for the potential variability of drug effects and safety. This variability may derive from:

- Different botanical raw material and controls which may influence or be influenced by the following (e.g., good agricultural and collection practices) (World Health Organization, 2003).

- Harvest location (including global positioning system (GPS) coordinates), growth conditions, stage of plant harvest, and harvest time/season – as these all impact the chemical profile.
- Post-harvest processing (e.g., washing, drying, and grinding processes), including control of foreign matter (i.e., inorganic and organic contaminants like soil, insects, and algae/fungi); preservation procedures; handling, transportation, and storage conditions; tests for elemental impurities; microbial limits; tests for residual pesticides, including parent pesticides and their major toxic metabolites; and tests for adventitious toxins (e.g., aflatoxins), foreign materials, and adulterants.

Processing of marijuana and its use in further manufacturing can lead to a range of forms that individuals may use or consume, including crude mixtures and highly purified substances of botanical origin, many of which may be cannabinoid compounds. Among known cannabinoids in the cannabis plant, both Δ^9 -THC (National Center for Biotechnology Information, 2023a) and Δ^8 -THC (National Center for Biotechnology Information, 2023e) produce marijuana's psychoactive effects. Because Δ^9 -THC is significantly more abundant than Δ^8 -THC, marijuana's intoxicating effects are largely attributed to the former. Only small quantities of Δ^8 -THC acid (Krejčí & Šantavý, 1975) and Δ^8 -THC (Hively et al., 1966) have been identified in plants (Thomas & ElSohly, 2016a). Δ^9 -THC is a resinous substance, essentially insoluble in water and extremely lipophilic, that is also photolabile and volatilized when exposed to heat (ElSohly, 2007). Furthermore, Δ^9 -THC is an optically active substance with two chiral centers at C-6a and C-10a and thus has four diastereomers (Schafroth et al., 2021), which are:

- (6aR,10aR)-6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydrobenzo[c]chromen-1-ol
 - alternate name: (-)-*trans*- Δ^9 -THC (National Center for Biotechnology Information, 2023b)
- (6aS,10aR)-6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydrobenzo[c]chromen-1-ol
 - alternate name: (-)-*cis*- Δ^9 -THC (National Center for Biotechnology Information, 2023f)
- (6aS,10aS)-6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydrobenzo[c]chromen-1-ol
 - alternate name: (+)-*trans*- Δ^9 -THC (National Center for Biotechnology Information, 2023d)
- (6aR,10aS)-6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydrobenzo[c]chromen-1-ol
 - alternate names: (+)-*cis*- Δ^9 -THC; (+)- Δ^9 -*cis*-THC (6aR, 10aS)-3 (National Center for Biotechnology Information, 2023c)

The formation of the (-)-*trans* isomer is favored in the plant and this isomer is 6–100 times more potent pharmacologically than the (+)-*trans* isomer (Brenneisen, 2007; Dewey et al., 1984).

As discussed in Section I, Background, the 2018 Farm Bill changed how the cannabis plant is scheduled under the CSA and removes hemp from the definition of marihuana. However, the term 'cannabis' is still often broadly used to refer to a wide variety of products manufactured from the *C. sativa* plant regardless of control status. These products may include the dried inflorescences (flowers), leaves, seeds, and stems and may be used in the manufacturing of concentrates, edibles, and topicals. Thus, marijuana or derived products can generally be categorized as one of four types:

- Flowers – includes dried herb that is smoked or vaped, and pre-rolls

- Concentrates – includes products for inhalation referred to as shatter, wax, butter, sugar, hash, resin, and rosin via vaping (use of an electronic vaporizer) or via dabbing (use of other paraphernalia such a pipe or “dab rigs”) (Colorado Department of Revenue, 2021; Drug Enforcement Administration, 2023)
- Edibles – includes infused food, beverage, and tincture products (e.g., baked goods, chocolate, drinks, candies, and snacks)
- Topicals – includes infused ointments, lotions, creams, or transdermal products

As a result of the 2018 Farm Bill, a large “hemp marketplace” exists,⁸ containing a wide variety of products representing the above product categories and involving various routes of administration. Aside from products purporting to meet the definition of hemp, the public also has access to cannabis products within the CSA definition of marijuana through state-authorized adult-use (i.e., nonmedical use) and medical-use programs, as well as via the illicit marketplace (see Factor 4 for additional details).

Based on these diverse sources of marijuana, there is a lack of unified controls on cultivation and manufacturing, which raises concerns related to the safety, quality, and consistency of botanical substances (e.g., botanical raw materials, extracts, and intermediates) and final product formulations that are currently accessed for medical and nonmedical use. Products sourced from state-authorized adult-use and medical-use programs are subject to a patchwork of inconsistent product standards and safety requirements. While each state program generally has a set of standards (for example, on manufacturing, testing, labeling, and packaging), each program’s controls are different, leading to wide variation of products across state-authorized programs. Additionally, the illicit marketplace is not subject to any standards or oversight. Thus, the range of products within the CSA’s definition of marijuana encompasses a large degree of variation in forms for consumption, composition of biologically relevant constituents, potency, and contaminants.

In conclusion, marijuana has hundreds of chemovars containing variable concentrations of Δ^9 -THC, cannabinoids, and other compounds. Thus, marijuana is not a single chemical with a consistent and reproducible chemical profile or predictable and consistent clinical effects. This current evaluation of marijuana will focus to greatest extent possible on wide-ranging cannabis plant-derived substances that are vehicles for the self-administration of Δ^9 -THC as the key biologically active substance on which the CSA’s current definition of marijuana is based.

Human Pharmacokinetics of Δ^9 -THC

The pharmacokinetics of Δ^9 -THC in humans have been evaluated following inhaled administration of marijuana and oral administration of marijuana. These are the most frequently used routes of administration for marijuana or isolated Δ^9 -THC (Vinette et al., 2022), as confirmed by the United States Poison Centers National Poison Data System (NPDS), which showed that ingestion (57%) and inhalation (41%) were the most common routes of administration for marijuana, while other routes of abuse were not common (<0.2%).

⁸ Additionally, hemp products with industrial applications, such as textiles, plastics, and other building materials, exist in the marketplace. However, these products are not relevant to this analysis.

Absorption of $\Delta 9$ -THC Following Inhaled Administration of Marijuana

Marijuana is commonly administered by humans via inhalation through smoking and, more recently, through vaping (e.g., heating and inhalation of botanical matter or other volatile substances containing $\Delta 9$ -THC) (Miech et al., 2019; Miech et al., 2020). Characterization of the pharmacokinetics of $\Delta 9$ -THC from smoked and vaped marijuana is difficult under naturalistic conditions because the pace of drug inhalation varies widely among individuals (Agurell et al., 1986; Herning et al., 1986; Huestis, Sampson, et al., 1992). For example, experienced marijuana smokers will titrate their $\Delta 9$ -THC dose to obtain the desired acute psychological effects and minimize undesired effects. Nonmedical marijuana users will also often hold marijuana smoke in their lungs for an extended period of time in an attempt to increase absorption and subsequent psychoactive effects despite data showing that this technique has minimal effects on $\Delta 9$ -THC plasma levels and subjective ratings of “high” (Azorlosa et al., 1995; Zacny & Chait, 1989, 1991). Thus, in order to standardize drug administration in scientific studies in humans, investigators will often use a Paced Inhalation Procedure (Foltin et al., 1987). Using this method, subjects take 5 seconds to prepare for inhalation, 5 seconds to inhale, 10 seconds to hold smoke or vapor in the lungs, followed by exhalation, and a 40 second interval prior to the next prepare/inhale/hold cycle.

Pulmonary administration of a drug is the route that produces the fastest rate of drug absorption, even faster than that produced by intravenous administration. Inhaled marijuana results in absorption of $\Delta 9$ -THC through the lungs in the form of an aerosol within seconds. Peak plasma levels of $\Delta 9$ -THC following inhalation occur very quickly, within 6-10 minutes (Grotenhermen, 2003). Psychoactive effects begin immediately following absorption, although peak subjective effects do not coincide with peak plasma $\Delta 9$ -THC levels and are often delayed (Singla & Block, 2022). Following administration of marijuana through inhalation, the bioavailability of $\Delta 9$ -THC is 10% to 35% (Grotenhermen, 2003; Lindgren et al., 1981). Although pulmonary administration does not involve dose loss from the hepatic first-pass effect in the liver, as would be seen with oral administration, the relatively low and variable bioavailability following inhaled marijuana results from significant loss of $\Delta 9$ -THC in side-stream smoke, cannabinoid pyrolysis, incomplete absorption of inhaled smoke or vapor, and metabolism in the lungs. An individual's experience and technique with smoking marijuana also determines the dose absorbed (Herning et al., 1986; Johansson et al., 1989).

Absorption of $\Delta 9$ -THC Following Oral Administration of Marijuana

After oral administration of $\Delta 9$ -THC, marijuana, or marijuana-infused foods (e.g., brownies) the onset of effects starts within 30 to 90 minutes, reaches its peak at 1.5 to 3 hours and remains measurable for 4 to 12 hours (Adams & Martin, 1996; Agurell, 1984; Agurell et al., 1986; Grotenhermen, 2003; Vandrey et al., 2017). Due to the delay in onset of effects after oral administration, including a slower onset of peak effects, titration of oral $\Delta 9$ -THC doses is difficult compared to inhalation of marijuana (Spindle et al., 2021). Oral bioavailability of $\Delta 9$ -THC, following ingestion of an edible containing marijuana or isolated $\Delta 9$ -THC, ranges from 5 and 20% (Agurell, 1984; Agurell et al., 1986). The low and variable oral bioavailability of $\Delta 9$ -

THC is a consequence of its first-pass hepatic elimination from blood and erratic absorption from stomach and bowel (Sharma et al., 2012). Ingestion of brownies containing marijuana also results in lower Δ^9 -THC plasma levels relative to inhalation of marijuana (Schlitz et al., 2020). Inter- and intra-subject variability occurs even with repeated dosing under controlled conditions.

Distribution, Metabolism and Excretion of Δ^9 -THC

Although there are differences in absorption of Δ^9 -THC depending on route of administration, the distribution, metabolism, and excretion of Δ^9 -THC is similar regardless of how the drug is administered.

Plasma concentrations of Δ^9 -THC decrease quickly after absorption through rapid distribution into tissues and through liver metabolism. Given that Δ^9 -THC has high lipophilicity, the apparent volume of distribution of Δ^9 -THC is high (10 L/kg) (Cerne, 2020) as it is distributed initially into organs such as lung, heart, brain, and liver that are highly perfused (Huestis, 2007). Over time with regular exposure to marijuana, Δ^9 -THC will concentrate and be retained in fat.

Metabolism of Δ^9 -THC occurs primarily via cytochrome P450 isozymes (CYP2C9, CYP2C19, and CYP3A4) (Lucas et al., 2018) via microsomal hydroxylation to both active and inactive metabolites (Agurell et al., 1986; Hollister, 1988; Lemberger, Crabtree, et al., 1972; Lemberger et al., 1970; Lemberger, Weiss, et al., 1972). The primary active metabolite of Δ^9 -THC is 11-hydroxy- Δ^9 -THC (Agurell et al., 1986; Lemberger & Rubin, 1975).

Plasma clearance of Δ^9 -THC approximates hepatic blood flow at about 950 ml/min or greater. The rapid disappearance of Δ^9 -THC from blood is largely due to redistribution to other tissues in the body, rather than to metabolism (Agurell, 1984; Agurell et al., 1986). Metabolism in most tissues is relatively slow or absent. Slow release of Δ^9 -THC and other cannabinoids from tissues and subsequent metabolism results in a long elimination half-life.

The plasma half-life of Δ^9 -THC following pulmonary administration varies based on frequency of use. Thus, in periodic users, the half-life is 1 to 3 days while in chronic users, the half-life is 5 to 13 days (Huestis, Henningfield, et al., 1992). After smoking, Δ^9 -THC venous levels decline precipitously within minutes and continue to decline to 5-10% of the peak level within an hour (Agurell et al., 1986; Huestis, Henningfield, et al., 1992; Huestis, Sampson, et al., 1992). In addition to 11-hydroxy- Δ^9 -THC, some inactive carboxy metabolites have terminal half-lives of 50 hours to 6 days or more. The latter substances serve as long-term markers in urine tests for earlier marijuana use.

The majority of the absorbed Δ^9 -THC dose is eliminated in feces, and about 33 percent in urine. Δ^9 -THC enters enterohepatic circulation and undergoes hydroxylation and oxidation to 11-nor-9-carboxy- Δ^9 -THC. The glucuronide is excreted as the major urine metabolite along with about 18 non-conjugated metabolites. Frequent and infrequent individuals who use marijuana metabolize Δ^9 -THC similarly (Agurell et al., 1986).

In conclusion, the pharmacokinetic profile of marijuana varies greatly depending on route of administration. Inhalation of marijuana produces a rapid increase in plasma levels of $\Delta 9$ -THC and an immediate onset of psychological effects. In comparison, oral administration of marijuana produces a much slower increase in plasma levels of $\Delta 9$ -THC and onset of psychological effects. Once $\Delta 9$ -THC has been absorbed, however, the metabolism and excretion of $\Delta 9$ -THC follows a standard path, although the half-life of $\Delta 9$ -THC may vary depending on frequency of use.

Currently Accepted Medical Use of Marijuana

To inform its scheduling recommendation, HHS has conducted an evaluation of whether marijuana has a CAMU for purposes of scheduling under the CSA, 21 U.S.C. § 812(b). Such an evaluation is one of the findings relevant to the placement of a substance in one of five drug control “schedules” set forth in 21 U.S.C. § 812(b).

In evaluating CAMU when considering whether to recommend rescheduling of marijuana, HHS (acting through the FDA and NIDA) applied a two-part test (hereinafter, “CAMU test”) that takes into account the current widespread medical use of marijuana under the supervision of licensed HCPs under state-authorized programs. Under Part 1 of the CAMU test, OASH considered whether there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented state-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these state jurisdictions. Part 2 of the CAMU test evaluated whether there exists some credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied. FDA’s evaluation in Part 2 is not meant to be, nor is it, a determination of safety and efficacy under the Federal Food, Drug, and Cosmetic Act’s (FD&C Act’s) drug approval standard for new human or animal drugs. Rather, the two-part test is to determine whether a substance, in this case marijuana, has a CAMU for purposes of drug scheduling recommendations and placement in a drug schedule consistent with criteria set forth in 21 U.S.C. 812(b).

In the evaluation and assessment under Part 1 of the CAMU test, OASH found that more than 30,000 HCPs are authorized to recommend the use of marijuana for more than six million registered patients, constituting widespread clinical experience associated with various medical conditions recognized by a substantial number of jurisdictions across the United States. For several jurisdictions, these programs have been in place for several years, and include features that actively monitor medical use and product quality characteristics of marijuana dispensed. OASH, through the Assistant Secretary for Health, concluded that, taken together, the findings from Part 1 warranted an FDA assessment under Part 2 of the CAMU test to determine if there exists credible scientific support for the use of marijuana for at least one of the medical conditions identified by OASH under Part 1.

FDA conducted Part 2 of the CAMU test for seven indications, based in part on OASH's findings under Part 1 of the CAMU test⁹ and in part on FDA's own analysis of the landscape in which marijuana is currently used medically, including information from state-authorized programs on how and to what extent marijuana is being utilized for medical purposes. The seven indications are: anorexia,¹⁰ anxiety,¹¹ epilepsy, inflammatory bowel disease (IBD), nausea and vomiting, pain, and post-traumatic stress disorder (PTSD). FDA's evaluation under Part 2 of the CAMU test was based on systematic reviews of studies investigating the safety and effectiveness of marijuana, relevant professional societies' position statements, data from state medical marijuana programs and United States national surveys, and the labeling of FDA-approved products relevant to the analysis.

In evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors considered in favor of a positive finding included whether: 1) favorable clinical studies of the medical use of marijuana, although not necessarily adequate and well-controlled clinical studies that would support approval of a NDA, have been published in peer-reviewed journals and/or 2) qualified expert organizations (e.g., academic groups, professional societies, or government agencies) have opined in favor of the medical use or provided guidance to HCPs on the medical use. Factors considered that weigh against a finding that Part 2 of the CAMU test is met included whether: 1) data or information indicate that medical use of the substance is associated with unacceptably high safety risks for the likely patient population, e.g., due to toxicity concerns; 2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; and/or 3) qualified expert organizations (e.g., academic or professional societies, government agencies) recommend against the medical use of marijuana (based on the available data at the time of their position statement).

Our review of the available information identified mixed findings of effectiveness across indications, ranging from data showing inconclusive findings to considerable evidence in favor of effectiveness, depending on the source. The largest evidence base for effectiveness exists for marijuana use within the pain indication (in particular, neuropathic pain). For the pain indication, a systematic review of scientific and medical literature was conducted this year by the

⁹ In Part 1 of the CAMU test, OASH identified at least 15 medical conditions where there is widespread current experience with medical use of the substance in the United States by licensed HCPs operating in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine. These conditions include amyotrophic lateral sclerosis (ALS), autism, cachexia, cancer, chronic pain, Crohn's disease, epilepsy or condition causing seizures, glaucoma, HIV/AIDS, multiple sclerosis, Parkinson's disease, persistent/severe muscle spasm, persistent/severe nausea, PTSD, and spasticity. FDA conducted Part 2 of the analysis for the medical conditions identified by OASH that were likely to have the most robust evidence available for review; because the analysis concluded that the Part 2 test has been met for at least one of the conditions identified in Part 1, there was no need to analyze all of them.

¹⁰ The anorexia indication reflects anorexia due to a medical condition (e.g., HIV/AIDS) and does not represent anorexia nervosa.

¹¹ While anxiety was not one of the specific medical conditions identified by OASH, it was included in FDA's Part 2 analysis based on a review of state-level usage data. Anxiety was considered of importance to evaluate given the reported prevalence of marijuana use in the treatment of anxiety symptoms regardless of its legal status in a given jurisdiction.

University of Florida (UF) under contract with FDA. UF epidemiologists identified some data supporting effectiveness of marijuana, including some within their own meta-analysis; however, they ultimately concluded the results are inconclusive or mixed. FDA also conducted a separate review of published scientific reviews. Several of those reviews drew conclusions similar to UF. In contrast, numerous other systematic reviews concluded that there exists some level of evidence supporting the use of marijuana for painful conditions. Other reviews, such as the (National Academies of Sciences & Medicine, 2017), concluded there was “substantial evidence”¹² supporting the use of cannabis products relevant to this review for pain. The Agency for Healthcare Research and Quality’s (AHRQ) living systematic review has concluded that there is some support for the use of marijuana-related products in the treatment of pain, but overall concluded these effects were small and the increased risk of dizziness, nausea, and sedation may limit the benefit.

UF evaluated other therapeutic conditions mentioned above, i.e., anorexia, anxiety, epilepsy, inflammatory bowel disease (IBD), nausea, and PTSD, employing a similar systematic review of scientific and medical literature. UF found that there is low- to moderate-quality evidence¹³ supporting the use of marijuana as medical treatment for outcomes in anorexia, nausea and vomiting, and PTSD. However, FDA review of systematic reviews showed mixed results for these indications. In particular, FDA found that the potential for psychiatric adverse events associated with treating PTSD with marijuana may be more substantial than any limited benefit in observational studies. Although UF did not conclude that there was evidence in support of the effectiveness of marijuana in IBD, both their review and other systematic reviews found some benefit with respect to subjective symptoms in this condition. With regard to epilepsy and anxiety, both UF’s review and FDA’s review of other systematic reviews did not find support for marijuana providing benefit in the treatment of these conditions. Where positive results on effectiveness outcome measures were found, the effects and the quality of evidence were generally in the low-to-moderate range. UF did not find high quality evidence supporting worsening of outcomes in any indication.

None of the evidence from the systematic reviews included in our CAMU Part 2 analysis identified any safety concerns that would preclude the use of marijuana in the indications for which there exists some credible scientific support for its therapeutic benefit. The clinical safety data identified in the literature from controlled trials were generally consistent between sources but limited in the rigor of safety reporting. The vast majority of the observational studies evaluated in the context of medical use were excluded from the final synthesis of evidence due to concerns regarding their quality (only one observational study for the anxiety indication and one for the PTSD indication were included). Generally, data on safety from both clinical trials and observational studies were scarce. Literature shows marijuana has more AEs when compared to a placebo or active control group, however, typically in the mild to moderate severity range. Severe AEs were uncommon.

¹² The term “substantial evidence” refers to language used within the NASEM report (2017) and is not meant to represent “substantial evidence” as defined in 21 USC 355(d).

¹³ UF determined the quality of evidence rating in accordance to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach described in the Cochrane handbook. For further details, please refer to the Section II.4.2.1 in this document.

FDA also reviewed results from state reporting data from 37 states with medical marijuana programs and surveys of patients using marijuana in Maryland and Minnesota, which had data available for review. Surveys of patients using marijuana in these two states found most patients did not report any side effects and those that did report side effects mostly described them as mild. Neither state's databases included patients who chose to stop using marijuana, which may result in an overestimation of positive experiences.

To date, real-world data sources available to FDA, in general, lack the necessary elements to identify the exposure (i.e., marijuana), to distinguish the reason for use (medical vs. recreational) and, if applicable, the condition that prompted its medical use, and/or to permit sound inferential analyses. Therefore, they were not included in this review.

Data from United States national surveys, in general, lacked details on patient characteristics and factors that prompted the use of marijuana for medical purposes, and data collection for these surveys was impacted by the coronavirus disease of 2019 (COVID-19) pandemic. Despite these limitations, these data suggested that medical use of marijuana increases as age increases. Only data from one survey provided information on the intended indication for use, suggesting that individuals often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms, but only approximately half of them reportedly had ever asked a healthcare professional for a recommendation to use medical marijuana.

Additionally, although the safety data obtained from use in a medical context are considered to be the most relevant for the CAMU analysis, FDA evaluated the safety of marijuana in the nonmedical setting to inform the potential for more severe outcomes. Specifically, FDA evaluated safety outcomes related to marijuana use in the setting of nonmedical use, use of uncertain intent, and unintentional exposure through a variety of epidemiological data sources and in relation to several comparator substances controlled under the CSA, including drugs in Schedule I: heroin (an illicit opioid drug); Schedule II: hydrocodone and oxycodone (approved opioid prescription drug products), cocaine and fentanyl (largely illicitly produced drugs in the nonmedical use setting, although there are approved prescription drugs); Schedule III: ketamine (an approved prescription drug); and Schedule IV: zolpidem, benzodiazepines, and tramadol (approved prescription drugs) (FDA Office of Surveillance and Epidemiology, 2023). The comparative data demonstrate that, even in the context of nonmedical use, marijuana has a less concerning overall safety profile relative to the comparators for a number of important outcomes (e.g., single substance use overdose death, hospitalizations). However, in young children, population-adjusted rates of ED visits and hospitalizations involving marijuana poisoning were higher than heroin, cocaine, and benzodiazepines for the periods studied. Of note, some of the comparator substances are approved for use in conditions similar to the indications for which marijuana was evaluated in the CAMU analysis (e.g., opioids for pain, benzodiazepines for anxiety-related conditions).

FDA also considered position statements from professional organizations relevant to the indications discussed. The vast majority of professional organizations did not recommend the use of marijuana in their respective specialty; however, none specifically recommended against

it, with the exception of the American Psychiatric Association (APA), which stated that marijuana is known to worsen certain psychiatric conditions.

On balance, the available data indicate that there is some credible scientific support for the use of marijuana in the treatment of pain, anorexia related to a medical condition, and nausea and vomiting, with varying degrees of support and consistency of findings. Additionally, no safety concerns were identified in our review that would indicate that medical use of marijuana poses unacceptably high safety risks for the indications where there is some credible scientific evidence supporting its therapeutic use.

Conclusions of CAMU

Based on the totality of the available data, we conclude that there exists some credible scientific support for the medical use of marijuana in at least one of the indications for which there is widespread current experience in the United States, as identified by OASH under Part 1 of the CAMU test. Seven indications were selected for evaluation under Part 2 of the CAMU test based on conclusions from Part 1 of the CAMU test as well as the FDA's analysis of the landscape of medical use of marijuana. The indications evaluated anorexia related to a medical condition, anxiety, epilepsy, inflammatory bowel disease, nausea and vomiting (e.g., chemotherapy-induced), pain, and post-traumatic stress disorder. The analysis and conclusions on the available data are not meant to imply that safety and effectiveness have been established for marijuana that would support FDA approval of a marijuana drug product for a particular indication. However, the available data do provide some level of support for the way marijuana is being used in clinical practice. Thus, based on the widespread HCP experience and the extent of medical use evaluated by OASH under the Part 1 test, and an evaluation of available credible scientific support described herein for at least some therapeutic uses identified in the Part 1 test, we find that that, for purposes of the drug scheduling criteria in 21 U.S.C. 812(b), marijuana has a CAMU in the United States for: anorexia related to a medical condition; nausea and vomiting (e.g., chemotherapy-induced); and pain.

FACTOR 4. ITS HISTORY AND CURRENT PATTERN OF ABUSE

Under the fourth factor, the Secretary must consider the history and patterns of marijuana use, including in relation to relevant comparator substances that are abused. This factor considers the federal and state-level history of marijuana control, marijuana sources for nonmedical and medical use, marijuana use in the United States since passage of the CSA, and current patterns of use and abuse of marijuana.

Federal History of Marijuana Control

The national history of marijuana in the United States includes its medical and nonmedical use, as well as legislation to control its use. Marijuana (as “an alcoholic extract of the dried tops of *Cannabis sativa*”) was described in the United States Pharmacopoeia as early as 1850 (Brinckmann et al., 2020). With the passage of the Pure Food and Drug Act in 1906, drugs such as marijuana, alcohol, heroin, morphine, and cocaine began to be characterized by the federal

government as “addictive” and/or “dangerous” (Wood, 1985). At that time, these drugs were frequently included in patent medicines, often without the consumer’s knowledge. After the new law was enacted, it required accurate reporting on a drug label about the drug substance and dose contained in the medication. This law, however, did not prohibit the sale or possession of “addictive” and/or “dangerous” drugs, including marijuana. As nonmedical use of marijuana and opioids became more popular in the United States, Congress provided funding in 1929 for two “narcotic farms” in Lexington, Kentucky, and Fort Worth, Texas, which were medical treatment centers run by the Public Health Service (PHS) for federal prisoners who were “habitual users of narcotics,” which included marijuana-derived products (Campbell, 2006). In 1931, the importation of marijuana into the United States began to be restricted under the Pure Food and Drug Act, except for medicinal purposes (Musto, 1972).

In order to further restrict nonmedical use of marijuana, the Federal Bureau of Narcotics campaigned for passage of the Marihuana Tax Act of 1937, which stated that, “Every person who imports, manufactures, produces, compounds, sells, deals in, dispenses, prescribes, administers, or gives away marihuana” would need to be registered and pay specified taxes (Anslinger, 1951). These taxes applied equally to healthcare providers as they did to manufacturers, and were considered extremely high, especially in the middle of the Great Depression. This led the American Medical Association to oppose the Marihuana Tax Act, since it restricted medicinal access to marijuana. During deliberations on the bill, which emphasized that marijuana was a dangerous drug, Dr. Walter L. Treadway of the Division of Mental Health at PHS (the precursor to the National Institute of Mental Health) provided testimony to Congress (Musto, 1972), stating that marijuana:

... does not produce dependence as in opium addiction. In opium addiction there is a complete dependence and when it is withdrawn there is actual physical pain which is not the case with cannabis. Alcohol more nearly produces the same effect as cannabis in that there is an excitement or a general feeling of lifting of personality, followed by a delirious stage, and subsequent narcosis. There is no dependence or increased tolerance such as in opium addiction. ... As with alcohol, it may be taken a relatively long time without social or emotional breakdown. Marihuana is habit forming although not addicting in the same sense as alcohol might be with some people...

Despite these criticisms, the Marihuana Tax Act was passed. Subsequently, the taxes imposed by the Marihuana Tax Act effectively prohibited marijuana use for medical, nonmedical, scientific, or industrial purposes (U.S. Customs and Border Protection, 2019). Five years later, marijuana was removed from the United States Pharmacopoeia in 1942 (Downs, 2016). With the passage of the Boggs Act of 1951, mandatory minimums lengthened the average sentence for first time marijuana offenders to 2 to 5 years, similar to that for opioid offenses, regardless of whether the individual was a nonmedical user or a trafficker (Tallaksen, 2019). The Narcotic Control Act of 1956 increased the minimum sentence for a first offender for marijuana to 2 to 10 years (Courtwright, 2004).

Despite the legal consequences, nonmedical marijuana use increased dramatically in the 1960s, especially among youth (National Academies of Sciences & Medicine, 2017). In 1969, the United States Supreme Court determined that the Marihuana Tax Act was unconstitutional in *Leary v. United States* because the law violated the Fifth Amendment right against self-

incrimination (Carroll, 1969). The following year, in 1970, Congress passed Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, which is commonly known as the CSA. The CSA effectively repealed all previous federal drug laws, including the Marihuana Tax Act, and provided a unified framework for control of drugs with abuse potential. When the CSA was enacted, marijuana was placed into Schedule I, which prohibited use of marijuana for medicinal or nonmedical purposes. This placement was consistent with the criteria established by the CSA under Section 202(b).

State-Level History of Marijuana Control

Changes in state-level marijuana laws in the United States in the modern era began in 1996 with the passage of California's Proposition 215, the Compassionate Use Act. This law legalized the use, possession, and cultivation of marijuana for treatment of patients with cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief, as long as they had a recommendation from their physician. Under the law, marijuana could also be cultivated by patient caregivers.

Since that time, as of August 2023, state-level laws allowing medicinal use of marijuana have been passed in a total of 38 states plus the District of Columbia: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Hawaii, Illinois, Kentucky,¹⁴ Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Utah, Vermont, Virginia, Washington, and West Virginia. Legalization of medical use of marijuana occurred through the action of 20 state legislatures and by 18 ballot measures.

In 2012, state-level legalization of nonmedical use of marijuana occurred for the first time in the United States in Colorado and Washington. Since then, state-level legalization of nonmedical use of marijuana occurred in a total of 23 states and the District of Columbia: Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Virginia, and Washington. Nonmedical use of marijuana occurred by ballot initiatives in 13 states and by state legislatures in nine states.

Marijuana Sources for Nonmedical and Medical Use

Products containing marijuana or derived from marijuana are generally obtained by the public from four main sources:

- State-authorized adult-use (nonmedical) programs
- State-authorized medical-use programs
- Illicit marketplace – includes unregulated smoke/vape shops, gas stations, convenience stores, marijuana clubs/lounges, person to person sales, and illicit cultivation (see also Factor 5, “National Forensic Laboratory Information System” section)
- Home cultivation for personal use (either legal or illegal under state programs)

¹⁴ When the supporting documents associated with the evaluation under the CAMU test were finalized, Kentucky had not yet legalized medicinal use of marijuana.

Individuals in the United States have access to a wide variety of marijuana and marijuana-derived products for purchase that are diverse in their potency, composition, and forms that dictate use through various routes of administration. The availability of these marijuana products varies across the three main sources above. Marijuana products can generally be categorized as one of four types:

- Flowers – includes dried herb that is smoked or vaped, and pre-rolls
- Concentrates – includes products for inhalation referred to as shatter, wax, butter, sugar, hash, resin, and rosin via vaping (use of an electronic vaporizer) or via dabbing (use of other paraphernalia such a pipe or “dab rigs”) (Colorado Department of Revenue, 2021; Drug Enforcement Administration, 2023)
- Edibles – includes infused food, beverage, and tincture products (e.g., baked goods, chocolate, drinks, candies, and snacks)
- Topicals – includes infused ointments, lotions, creams, or transdermal products

In the epidemiological data described below, the broad range of products that are marijuana or marijuana-derived may not be identified fully in terms of being from certain product categories or specific/multiple sources or being used by specific routes of administration.

Marijuana Use in the United States Since Passage of the CSA

Since 1970 when the CSA was passed, marijuana use has vacillated over time. As stated in the 2017 NASEM report *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*:

“The prevalence of cannabis use peaked in the late 1970s, when more than one-third of high school seniors (37 percent in 1976) and one in eight Americans over 12 years old (12.8 percent in 1979) reported past-month use (Johnston et al., 2016). Self-reported past-month use declined throughout the 1980s and by 1992 was just one-third of the 1970s peak, both among high school seniors (12.1 percent) and the general population (4.4 percent). The recorded decline in use did not last long. The mid-1990s saw rapid increases, with use by high school seniors nearly doubling within just the 5 years from 1992 (11.9 percent) to 1997 (23.7 percent). Throughout the late 1990s and early 2000s, the rates of use largely stagnated, with trends among youth and the general population moving roughly in parallel (Johnston et al., 2016).

“The years since 2007 have seen steady year-over-year increases in general population past-month use, rising from 5.8 percent to 8.4 percent in 2014 (a 45 percent increase). There is no single clear explanation for the post-2007 increases in use. Hypothesized causes include declining potency-adjusted prices on the illicit market; the proliferation of medical cannabis laws, especially those that allow for sale at brick-and-mortar dispensaries; and changing public perceptions about the harms of cannabis use (Sevigny et al., 2014).”

Gallup Poll data from 1969 to 2013 show a steady increase over time in response to a question regarding whether the respondent had personally tried marijuana (Saad, 2013). In 1969, there was a 4% affirmative response, which increased to 12% by 1973. By 1977, 24% of respondents

affirmed they had used marijuana, which increased to 33% in 1985. After this date, the percent of individuals who affirmed they had used marijuana was stable, with 34% in 1999 and 38% in 2013.

Current Patterns of Use and Abuse of Marijuana

In analyzing current patterns of use and abuse of marijuana and marijuana-derived products, epidemiological databases were analyzed from 2015 to the most recent years of available data (which varies among data sources). A wide variety of epidemiological databases provide necessary data for our analyses. These include the NSDUH, BRFSS, RADARS, NMURx, MTF, YRBSS, and ICPS. A description of each data source and a summary of the data from each source follows below.

These epidemiological evaluations of marijuana use were limited to products containing only botanical marijuana, including various forms of marijuana such as dried leaves rolled into cigarettes or smoked in pipes, edibles (e.g., brownies, cookies, tea), vaping oils, concentrates, and liquid marijuana extract. Cannabis-derived products with less than 0.3% Δ 9-THC (e.g., hemp, FDA-approved cannabidiol oral solution), synthetic cannabinoids that are intended to mimic Δ 9-THC, and marijuana-related FDA-approved drug products [Marinol (dronabinol), Syndros (dronabinol), Epidiolex (cannabidiol), and Cesamet (nabilone)] have been excluded from this analysis to the extent possible, although some respondents on these survey instruments could potentially conflate their use of these excluded products with “marijuana” when responding.

National Survey on Drug Use and Health

NSDUH is an annual, nationally representative, cross-sectional household survey of individuals ages 12 years and older that provides information on the use of drugs and alcohol in the United States (SAMHSA, 2022b). Since 2015, NSDUH has elicited information on any use of a drug (for nonmedical and medical uses combined), as well as on nonmedical use (called “misuse” in the database), of select prescription and illicit drugs in the past year. NSDUH defines misuse of a drug as “use in any way not directed by a doctor, including use without a prescription of one’s own; use in greater amounts, more often, or longer than told.” This definition of “misuse” includes use of a drug with therapeutic intent that is not the result of a recommendation from a health care provider, as well as intentional, non-therapeutic use of a drug to obtain a desired psychological or physiological effect (abuse). As a result of the public-health emergency resulting from the COVID-19 pandemic, NSDUH data collection was disrupted in 2020 and 2021, leading to trend breaks in these years. As a result, it is not possible to interpret trends on use of drugs or other substances from 2019 and years prior with 2020 and 2021 estimates, and it is not possible to combine estimates from 2020 with estimates from 2021.

Past-Year Use of Marijuana for Nonmedical and Medical Uses Combined

Based on NSDUH data, from 2015 to 2019 the past-year use of marijuana for any reason (nonmedical and medical) among people ages 12 years and older increased from 14 to 18%. This is in contrast to past-year use (nonmedical and medical) of comparator drugs that have

FDA-approved therapeutic indications, where use declined or remained relatively stable over the same timeframe, including hydrocodone (22 to 16%), benzodiazepines (12 to 11%, 2017 to 2019 only), oxycodone (11 to 9%), tramadol (7 to 6%), zolpidem (4 to 3%), and ketamine (less than 1%). The decline for hydrocodone was the largest for any comparator drug (~6%), and by 2019, the prevalence of any past-year use of marijuana exceeded that of hydrocodone (18% vs. 16%, respectively). Although there were trend breaks for the years 2020 and 2021, hydrocodone past-year use continued to decrease during these 2 years while marijuana past-year use continued to increase (13% vs. 19%, respectively, in 2021).

Past Year Use of Marijuana for Nonmedical Uses Only

Based on NSDUH data, from 2015 to 2019, the prevalence of past-year nonmedical use of marijuana (i.e., use without an HCP recommendation among people ages 12 years and older increased. This finding is based on an increase in the prevalence of overall nonmedical use of marijuana from 12 to 15% and on an increase in nonmedical use of marijuana only, without nonmedical use of other drugs that are abused, from 8% to 11% during this period. There was a slight decrease in both categories in 2020, but the prevalence increased again in 2021 (16% and 11%, respectively) to levels that were higher than those reported in 2019.

In contrast, the prevalence of past-year nonmedical use of comparator drugs was less than 3% for each drug, including heroin cocaine oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem, which is much less than that for marijuana, either alone or with other drugs. Over the 2015 to 2021 reporting period, the overall use of these comparator drugs declined slightly or remained fairly stable. Notably, the majority of individuals who reported nonmedical use of marijuana did not report nonmedical use of the comparator drugs.

Over the same reporting period of 2015 to 2021, the prevalence of past-year use of alcohol ranged from 62% to 65% for individuals ages 12 years and older, far exceeding the prevalence for marijuana or other comparator drugs.

These data demonstrate that alcohol has the highest prevalence of past-year only use, followed by nonmedical use of marijuana. The prevalence of the other comparators is far below that of alcohol and marijuana.

Prevalence of Past-Year Marijuana Use Without and With a Recommendation from Health Care Provider

The NSDUH data show that most individuals who used marijuana in the past year did not do so based on a recommendation from an HCP (i.e., they were using marijuana for nonmedical purposes). The yearly percentage of individuals who used marijuana but did not have an HCP recommendation ranged from 89% from 2015-2017, decreasing over time to 84% in 2020 and increasing slightly to 86% in 2021. During the same period, exclusive medical use of marijuana that was recommended by an HCP ranged from 7-8% from 2015-2019, increased to 10% in 2020, and decreased to 9% in 2021.

An evaluation of the frequency of past-year marijuana use showed that ~50% of those individuals without an HCP recommendation used marijuana for 60 or fewer days in the year. However, another 29% of those without an HCP recommendation used marijuana for more than 241 days in the year. In contrast, for those individuals whose use of marijuana was sometimes or always recommended by an HCP use, 51% and 55% (respectively) used marijuana at least 241 days in the year.

Prevalence of Past-Month Marijuana Use

The NSDUH data from 2021 show that among individuals who used any marijuana in the past year, 69% used marijuana in the past month, while 81% of those who used marijuana without nonmedical use of other drugs used marijuana in the past month. For comparator drugs, the percentage of individuals with past-year use who used each substance nonmedically in the past month was 76% for alcohol, 49% for heroin, 38% for cocaine, and 28% for ketamine.

Behavioral Risk Factor Surveillance System

BRFSS is a national, state-based, cross-sectional telephone survey by the Centers for Disease Control and Prevention (CDC) (CDC, 2021a, 2021b, 2022). The participants in the 2021 BRFSS module for marijuana included ~68 million individuals 18 years and older, residing in 24 states and territories: Alaska, Connecticut, Delaware, Hawaii, Idaho, Illinois, Indiana, Kentucky, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New York, North Dakota, Ohio, Oklahoma, Rhode Island, Utah, Vermont, Wyoming, and Guam.

The estimated prevalence of past month marijuana use for any reason in the BRFSS survey was 12%, with 88% reporting no marijuana use. Among those with past-month marijuana use, mean frequency of use was 17 days/month, with half of respondents reporting that they used marijuana 20 to 30 days/month. This pattern was consistent across all age categories and sex.

When the reason for use was evaluated, the percentage of individuals who reported use for both medical and nonmedical reasons was 39%, compared to 36% for those who reported use for nonmedical reasons only and 25% for those who reported use for medical reasons only. Those individuals who reported past-month use of marijuana for medical reasons were more likely to be adults 55 years and older, while individuals who reported past-month marijuana use for nonmedical reasons only were more likely to be younger adults aged 18 to 24 years.

Individuals who reported using marijuana in the past 30 days for both nonmedical and medical reasons were more likely (62%) to report marijuana use near daily (20-30 days/month) than individuals who reported marijuana use for nonmedical reasons only (34%). Similarly, individuals who used marijuana for medical reasons only were also more likely (57%) to report near daily use.

Researched Abuse, Diversion and Addiction-Related Surveillance System Survey of Nonmedical Use of Prescription Drugs

The RADARS System conducts the NMURx Program, a serial, cross-sectional, online survey of the general adult population (18 years and older) to elicit information on the nonmedical use of drugs (prescription, nonprescription, unapproved, and illicit) (Black et al., 2019; The Researched Abused, 2023). NMURx estimates represent measures of past-year drug use in an enriched sample of United States adults with higher-than-average nonmedical use of prescription pain relievers and illicit drugs.

Based on NMURx program, past-year use of marijuana was reported by 21% of individuals, while past-year use of comparator substances was substantially lower: benzodiazepines (4%), hydrocodone, oxycodone, tramadol (2% each), cocaine or crack (less than 2%) and illicit fentanyl, heroin, and ketamine (less than 1% each). This pattern of much greater marijuana use compared to other drugs is consistent with the patterns reported in NSDUH and BRFSS.

Monitoring the Future

MTF collects information on the use of selected prescription and illicit drugs and alcohol by conducting an annual, nationally representative, cross-sectional survey of 8th, 10th, and 12th graders in public and private schools (Miech et al., 2022; Miech et al., 2023). As a result of the COVID-19 pandemic, there is a potential trend break in the 2020 MTF data.

MTF data show that during the years 2012 to 2022, the illicit drug most frequently used by 12th grade students who reported past-year drug use was marijuana/hashish (~35% per year from 2012 to 2020, with a reduction to ~30% per year in 2021 and 2022). In contrast, in 2022, alcohol was used by 52% of 12th grade students within the last 12 months, similar to percentages in 2019 and 2020 (52% and 55%, respectively), but higher than the 2021 level of 47%. All other comparator drugs (hydrocodone, heroin, tramadol, cocaine, ketamine, and zolpidem) were each used in the past year by fewer than 5% of 12th graders from 2012 to 2022.

MTF data for past-month use showed a similar pattern. During the years 2012-2022, the illicit drug most frequently used by 12th grade students who reported past-month drug use was marijuana/hashish (~20-22% per year) compared to past-month use of cocaine (~1% per year) or heroin (less than 0.5% per year). However, past-month alcohol use by 12th grade students (28%) exceeded that of marijuana in 2022. MTF does not provide past-month use data for hydrocodone, heroin, tramadol, ketamine, or zolpidem.

MTF data show that for those 12th graders who used marijuana, cocaine or heroin in the past month, daily use of marijuana ranged from ~6-7%, compared to daily use of cocaine or heroin that was less than 1%. MTF does not provide past-month use data for hydrocodone, tramadol, ketamine, or zolpidem.

Youth Risk Behavior Surveillance System

YRBSS was established by the CDC and conducts school-based surveys every 2 years, in partnership with state, local, territorial, and tribal governments, with a focus on youth health behavior in the United States. The YRBSS high school component, the Youth Risk Behavior Survey, includes a nationally representative survey of 9th through 12th grade students (CDC, 2020, 2023; Underwood et al., 2020).

YRBSS data show that from 2009 to 2019, ~ 20% of students in 9th-12th grade reported using marijuana at least once in the past month during each year evaluated. When students 17 years and older were asked how old they were when they first used marijuana, 43% reported they initiated use between the ages of 15 to 16 years, 25% initiated use between 13 to 14 years, and 13% initiated use at 12 years of age and younger.

In contrast, past-month alcohol use by high school students (29%) in 2019 was greater than that of marijuana use, while past month prescription opioid misuse (including codeine, hydrocodone, or oxycodone) (7%) in 2019 was much lower than that of both alcohol and marijuana use.

International Cannabis Policy Study

ICPS conducted serial, cross-sectional surveys in 2019 to 2021 of individuals ages 16 to 65 years living in the United States to understand the public health impact of marijuana legalization (Hammond et al., 2022; ICPS, 2023). The present evaluation focused on respondents who reported at least some past-year marijuana nonmedical use (by indicating that they were not a medical marijuana user, defined as someone who uses marijuana only to treat a medical condition).

ICPS data show that the prevalence of past-year nonmedical use of marijuana ranged from 18% to 22% of individuals surveyed from 2019 to 2021, while the prevalence of past-month nonmedical use was lower, ranging from 12% to 14% of individuals surveyed. Individuals 26 to 34 years had the highest relative prevalence of nonmedical marijuana use, with 26% reporting past-year use and 18% reporting past-month use. This prevalence was higher than that of individuals ages 16-17, 18-25, and 35-64 years, where past-year use was 19-23% while past-month use was 12-13%.

When those individuals who reported past-year marijuana use in 2021 in ICPS were asked why they used the drug, 33% reported use for medical reasons, while 61% responded “no” to the question about past-year medical use and were classified as using marijuana for nonmedical reasons only. The percentages do not sum to 100% because of nonresponse.

When frequency of nonmedical use of marijuana was evaluated in ICPS for those individuals who used marijuana nonmedically at least once a year, individuals 16-17 years had the highest percentage of use less than once a month (~40%) compared to other age cohorts (~25-31%), while individuals 26-34 years had the highest percentage of daily use (~43%) compared to individuals in other adult cohorts (~34-37%) and to individuals 16-17 years (~24%).

Among individuals who nonmedically used marijuana in the past year, 49% never used alcohol and marijuana at the same time, while 35% sometimes used the two substances together, 9% often used them together, and 5% used alcohol every time they used marijuana.

Conclusions

When data on marijuana use from epidemiological databases are evaluated together, certain conclusions can be drawn about its current pattern of abuse.

From 2015 to 2019, NSDUH data show that the prevalence of past-year use of alcohol was 5-6 times greater than nonmedical use of marijuana. In contrast, the prevalence of past-year nonmedical use of heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem was 4-5 times less than that for marijuana nonmedical use. Similar past-year comparative drug use data were reported in RADARS-NMURx, in MTF, and in ICPS.

In NSDUH, among people with past-year marijuana use, approximately half of individuals reported nonmedical marijuana use an average of less than 5 days/month while another 30% reported nonmedical marijuana use for an average of more than 20 days/month. In the BRFSS population of people with past-30-day marijuana use, near-daily use was more likely if the individual was using marijuana for medical reasons in BRFSS data; however, medical-only use was less common (25% for medical use compared to 39% for medical and nonmedical use, and 36% for nonmedical use only). In NSDUH, past-month frequency of marijuana nonmedical use is less than what was reported in BRFSS for frequency of marijuana use for any reason (the mean frequency of use was 17 days and half of respondents reported that they used marijuana for any reason more than 20 days/month). Yet, the NSDUH population was younger (included people ages 12 years and older) and included people who used marijuana in the past year, not just within the past month, like in BRFSS. Additionally, in NSDUH, past-year use of marijuana was predictive of past-month use for 60-80% of respondents, similar to alcohol use (approximately 80% of those who used alcohol in the past year also did so in the past month).

These data show that use of marijuana for medical and nonmedical purposes is extensive in the United States, but that its prevalence of use is less than that of alcohol and significantly more than that of other drugs of abuse that are scheduled under the CSA.

FACTOR 5. THE SCOPE, DURATION, AND SIGNIFICANCE OF ABUSE

Under the fifth factor, the Secretary must consider the scope, duration, and significance of marijuana abuse, including in relation to relevant comparator substances that are abused. The consequences over time of marijuana abuse compared to the abuse of other substances are described based on data from the NPDS, NSDUH, TEDS, NAVIPPRO, NEDS, and NIS.

Epidemiological Data on Consequences of Marijuana Abuse

National Poison Data System

Data from America's Poison Centers' NPDS provide information on the scope of contacts with a poison center (PC) following marijuana abuse, relative to abuse of selected comparators (AAPCC, 2016; Gummin et al., 2022). (American's Poison Centers' National Poison Data System [NPDS] Data Definitions 2016 defines *moderate effect* as, "[t]he patient exhibited symptoms as a result of the exposure which are more pronounced, more prolonged or more of a systemic nature than minor symptoms" and defines *major effect* as "[t]he patient has exhibited symptoms as a result of the exposure which were life-threatening or resulted in significant residual disability or disfigurement.")

In order to quantify the scope and burden of PC cases involving abuse of marijuana and selected comparator drugs, the number of PC abuse cases for a substance (either alone or in combination with another substance) was analyzed for the period of 2015 to 2021. The highest number of PC abuse cases was observed for alcohol (n=56,143), followed by heroin (n=34,083) and by benzodiazepines (n=33,688). The fourth highest number of PC abuse cases was for marijuana (n=22,731), with all other comparators showing even fewer PC abuse cases: cocaine (n=15,196), oxycodone (n=12,683), hydrocodone (n=5,575), illicit fentanyl (n=3,636), tramadol (n=2,965), zolpidem (n=2,348), and ketamine (n=832).

When the PC abuse cases for 2015 to 2021 were analyzed for cases involving a single substance only, the rank order of PC abuse cases by number was the same as the order from all PC abuse cases for substances used alone or in combination with another substance, such that the highest number was still for alcohol (n=24,022), with heroin (n=21,970) and benzodiazepines (n=10,872) in second and third place. The fourth highest number of PC abuse cases for a single substance was still for marijuana (n=10,388), with all other comparators showing even fewer PC abuse cases: oxycodone (n=5,943), cocaine (n=4,242), hydrocodone (n=2,062), tramadol (n=1,398), illicit fentanyl (n=1,233), zolpidem (n=941), and ketamine (n=382).

In order to assess the proportion of PC cases that involve abuse (either alone or in combination with another substance), the number of PC abuse case counts for a substance was divided by the total number of PC cases for that substance, for the period of 2015 to 2021. This calculation showed that abuse cases made up the largest proportion of PC cases that involved illicit fentanyl (72%), heroin (65%), cocaine (41%) and ketamine (40%). The fifth highest percentage was for cases involving marijuana (36%), followed by alcohol (15%), oxycodone (13%), benzodiazepines (8%), hydrocodone (5%), tramadol (4%), and zolpidem (3%).

When a similar calculation was made to assess the prevalence of abuse cases contacting a PC based on adverse consequences associated with a single substance only for the same period, the three substances most likely to lead to a PC call following abuse were heroin (65%), oxycodone (47%), and tramadol (47%). The fourth highest percentage was for marijuana and ketamine (46%), followed by alcohol (43%), zolpidem (40%), hydrocodone (37%), illicit fentanyl (34%), benzodiazepines (32%), and cocaine (28%).

Annual utilization-adjusted abuse case rates were then calculated by dividing the number of PC abuse case counts by the prevalence of past-year use based on NSDUH estimates from people 12 years and older, for the period of 2015 to 2019. There were two calculations for each substance, based on two denominators: one for any past-year use of the substance and one for past-year

nonmedical use of the substance. These utilization-adjusted rates convey the likelihood that use of a drug will result in PC abuse cases when considering how many people use the drug for any reason or for nonmedical reasons.

When utilization-adjusted abuse rates (PC abuse cases per one million people with any past year use for a substance alone or with another substance) were calculated using data from 2015 to 2019, the highest rate was seen for heroin (increasing from 4038 to 7201 cases per one million people). The next highest rates were seen for ketamine (decreasing from 535 to 227 cases per one million people), cocaine (relatively stable at 375 to 389 cases per one million people), and benzodiazepines (relatively stable at 171 to 139 cases per one million people, 2018 to 2019 only), but these rates were considerably lower than the rate for heroin. The rates for marijuana (relatively stable at 75 to 70 cases per one million people) and oxycodone (relatively stable at 60 to 61 cases per one million people) were similar, as were the rates for alcohol (relatively stable at 47 to 41 cases per one million), zolpidem (relatively stable at 46 to 30 cases per one million people), tramadol (relatively stable at 36 to 19 cases per one million people) and hydrocodone (relatively stable at 23 to 13 cases per one million people). A similar pattern of utilization-adjusted abuse rates was seen among cases involving a single substance only during the same time period.

The most common routes of administration for single-substance PC abuse cases from 2015 to 2021 for all substances were primarily through oral ingestion and inhalation/nasal administration, with occasional parenteral administration (including intravenous), depending on the substance. As would be expected, alcohol was almost exclusively used orally by respondents (99%). Benzodiazepines, tramadol, zolpidem and hydrocodone were also nearly always used orally by respondents (97%, 97%, 96%, and 95%, respectively), although each of them also had a small degree of use via inhalation/nasal administration (3%, 2%, 4%, and 4%, respectively). Oxycodone use by respondents was 72% oral, 22% inhalation/nasal, and 4% parenteral. Marijuana was used orally by slightly more than half of respondents (57%) and was also used through inhalation/nasal administration by 41% of respondents. Cocaine and ketamine were both used orally by 37% of respondents, with a similar frequency of use through inhalation/nasal routes (40% and 37%, respectively) and lesser frequency of use through parenteral routes (6% and 12%, respectively). Finally, illicit fentanyl use was 24% oral and 28% through inhalation/nasal use. For those drugs where the route percentages do not add up to 100%, this is attributable to cases involving more than one route of abuse, small percentages observed for other routes of administration, and by large percentages where the route is unknown.

An analysis of medical outcomes, related to exposure based on severity, timing, and assessment of clinical effects, for all single-substance PC abuse cases involving marijuana or comparator drugs show that serious medical outcomes (a combination of moderate effect, major effect, and death) were greatest with illicit fentanyl (81%) and heroin (79%), followed by oxycodone (70%), ketamine (64%), tramadol (62%), cocaine (59%), hydrocodone (44%), marijuana (41%), benzodiazepines (32%), alcohol (31%), and zolpidem (27%). When the death rate was evaluated, the highest rate was for fentanyl (25%). Cocaine, heroin, and alcohol had very low rates (3%, 2%, and 2%, respectively) compared to fentanyl, with all other comparators reporting death rates less than 1% (oxycodone, hydrocodone, tramadol, ketamine, benzodiazepines, zolpidem, marijuana). However, out-of-hospital deaths are under-captured in NPDS so these

death rates cannot be broadly extrapolated to indicate the rate of death from adverse events involving these substances.

National Survey on Drug Use and Health

Data from NSDUH provide nationally representative information on the prevalence of substance use disorder (SUD) in 2021 among individuals aged 12 years or older who reported nonmedical use of marijuana in past year, in comparison to heroin, cocaine, or alcohol use in the past year. Drug-specific data on oxycodone, hydrocodone, fentanyl, tramadol, ketamine, benzodiazepines, and zolpidem were not available in the NSDUH analyses of SUDs. A diagnosis of SUD is made when an individual endorses at least 2 of the 11 criteria for SUD, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (e.g., has at least a mild severity of the SUD). Individuals are classified with a mild SUD if they meet two to three of the criteria, a moderate SUD if they meet four to five of the criteria, and a severe SUD if they meet six or more of the criteria.

NSDUH data show that among individuals with past-year heroin use in 2021, there was an 81% prevalence of meeting the criteria for a heroin SUD (i.e., endorsing at least 2 of the 11 criteria for SUD (according to DSM-V; severity data for heroin not available). In comparison, there was a 30% prevalence of meeting the criteria for marijuana SUD among individuals who used marijuana for nonmedical reasons only, with 17% of individuals with past-year nonmedical only use having a mild SUD, 8% having a moderate SUD, and 5% having a severe SUD. Data were also available on individuals who did not use other drugs illicitly and nonmedically used only marijuana, where there was a slightly lower prevalence of 24% for marijuana SUD, with 15% of individuals with past-year marijuana use having mild SUD, 6% of these having a moderate SUD, and 3% having a severe SUD. There was also a 30% prevalence of meeting criteria for cocaine SUD among individuals who used cocaine in the past year, with 13% of those with past-year cocaine use having a mild SUD, 5% having a moderate SUD, and 12% having a severe SUD. For those individuals who used alcohol in the past year, the prevalence of alcohol SUD was 17%, with 10% of individuals with past-year alcohol use having a mild SUD, 4% having a moderate SUD, and 3% having a severe SUD.

Although the 2021 NSDUH data show that the likelihood of meeting the criteria for a SUD was highest for heroin, followed by marijuana/cocaine, and alcohol, the absolute number of individuals who met criteria for the specific drug SUD had a different rank order. Thus, alcohol had the highest estimated number of individuals who met criteria for its specific SUD (~29,544,000), followed by marijuana (~13,078,000 people with marijuana nonmedical-only use, ~7,454,000 with nonmedical-only use and no nonmedical use of other drugs), cocaine (~1,408,000), and heroin (~894,000) for their specific SUDs.

Treatment Episode Data Set

TEDS is a database run by HHS' Substance Abuse and Mental Health Services Administration (SAMHSA) that presents information on the demographic and substance use characteristics of the annual admissions to treatment for alcohol and drug abuse in facilities that are licensed or certified by the States to provide substance abuse treatment and is required by the States to

provide TEDS client-level data (SAMHSA, 2022c). Since TEDS is based only on reports from these facilities, TEDS data do not represent the total national demand for substance abuse treatment or the prevalence of substance abuse in the general population. Additionally, TEDS is an admissions-based system, not an individual-based one, which means that an individual who is admitted to treatment twice within a given year would be counted as two admissions.

Out of 1.4 million admissions documented in the 2020 TEDS dataset, the most frequently reported primary drug of admission was alcohol (31%, n=442,014 admissions), followed by heroin (21%, n=292,126 admissions), marijuana (10%, n=139,481 admissions), and cocaine (5%, n=71,725 admissions). Other comparator drugs, including oxycodone, benzodiazepines, hydrocodone, ketamine, or tramadol, were each reported as the primary drug in less than 2% of admissions.

Over the reporting period of 2015 to 2020, the proportion of admissions with alcohol reported as the primary drug declined from 33% in 2015 to 30% in 2018 but increased slightly to 31% of admissions in 2019 and 2020. In comparison, the proportion of admissions with heroin reported as the primary drug was relatively stable from 2015 to 2018 (~26% for each year), declined to 23% in 2019 and declined further to 21% of admissions in 2020. The proportion of admissions with marijuana as the primary drug declined each year from 14% in 2015 to a low of 10% in 2020, while the proportion of admissions with cocaine as the primary drug increased slightly during this time from 5% in 2015 to 6% in 2019. During this reporting period, the other comparator drugs, oxycodone, benzodiazepines, hydrocodone, ketamine, and tramadol, were each reported as the primary drug in less than 2% of admissions each year.

In 2020, marijuana and cocaine were most likely to be reported as the secondary drug at admission (25% and 24%, respectively), followed by alcohol (15%), heroin (8%), and benzodiazepines (6%), with all other comparators reported as less than 2%. For tertiary drugs at admission, marijuana (29%) was reported most frequently, followed by cocaine (18%), alcohol (16%), and heroin (5%), with all other comparators reported as less than 2%.

National Addictions Vigilance Intervention and Prevention Program

NAVIPPRO is a surveillance system for substance use and nonmedical use of prescription medication in a convenience sample of adults seeking treatment or being assessed for substance use disorder treatment at participating facilities across the United States. NAVIPPRO Addiction Severity Index-Multimedia Version (ASI-MV) is a self-administered, computerized, validated clinical assessment tool that collects data on recent drug use behaviors for evaluation and treatment planning at intake (Butler et al., 2001).

From 2020 through 2021, there were a total of 76,249 NAVIPPRO ASI-MV assessments in individuals entering or being assessed for substance use disorder treatment at a center participating in the NAVIPPRO network. The drug most frequently endorsed for past-month use was marijuana (n=20,458; 27%), followed by alcohol (5 or more alcoholic drinks/day, n = 16,388; 22%), heroin (n=9,078; 16%), fentanyl (n=6,186; 8%), hydrocodone (n=3,448; 5%), oxycodone (n=3,186; 4%), cocaine and/or crack (n=5,417; 7%), tramadol (n=543, 1%), and ketamine (n=169; less than 1%).

Nationwide Emergency Department Sample

NEDS is the largest all-payer ED database in the United States, yielding national estimates of hospital-owned ED visits, as developed for HHS' AHRQ (AHRQ, 2022a, 2022c). NEDS is a sample of records from ED visits sourced from the State Emergency Department Databases, which captures discharge information on all ED visits that do not result in hospital admission, and the State Inpatient Databases, which contains information on patients first seen in the ED and then admitted to the same hospital. In 2020, the included sample of ED visits was sourced from 995 hospital-owned ED units and sourced from 41 states, accounting for 85% of the United States population. The unweighted NEDS sample in 2020 contains data from over 28 million ED visits, which resulted in a weighted estimate of 123 million ED visits. In this evaluation, ED visits that noted an alcohol, marijuana or cocaine-related disorder were compared. ED visits may not have been directly due to a specific substance-related disorder, but the patient was recorded as having had an alcohol, marijuana or cocaine-related disorder in the administrative claim associated with their ED visit. (A "substance-related disorder" refers to any one of a set of International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes that indicate abuse, dependence, or unspecified use of a specific substance (i.e., marijuana, cocaine or alcohol) or set of substances (i.e., opioids or stimulants). Since it cannot be determined if the ICD-10 code also included a substance use disorder diagnosis according to the DSM-V criteria, the term "substance-related disorders" is used in this review.

Based on NEDS data, from 2016 to 2020, the highest estimated number of annual ED visits were for an alcohol-related disorder, which rose slightly over this reporting period from ~4 million to ~4.1 million, with ~3.2 million estimated annual ED visits each year during this period that involved alcohol as a single substance. Over the 2016 to 2020 timeframe, estimated annual ED visits involving a marijuana related disorder increased from approximately 1.3 million to over 1.7 million, with the estimated annual ED visits for single substance marijuana increasing from 757,731 to 1.08 million. For cocaine, the estimated annual ED visits involving a cocaine-related disorder increased from 599,165 in 2016 to 774,737 in 2018, then declined to 664,641 in 2020, with the estimated annual ED visits for single-substance cocaine-related disorder ranging from 204,257 in 2016 to 225,566 in 2020, with an increase in estimated annual ED visits for 2017 to 2019 ranging from 261,155 to 266,614.

A utilization-adjusted rate of estimated ED visits was then calculated by dividing the estimated annual ED visits for each substance as reported in NEDS by the number of individuals reporting any past-year use of that substance as reported in NSDUH. The highest utilization-adjusted rate of estimated ED visits was observed for cocaine-related disorder, which ranged from 2016 to 2020 from 11,765 to 14,014 per 100,000 individuals, with the annual rate of single-substance ED visits ranging from 4,011 to 4,952 per 100,000 individuals. Marijuana had the second-highest utilization-adjusted rate of estimated ED visits from 2016 to 2020, where the rates for marijuana related disorder ranging from 3,472 to 3,940 per 100,000 individuals (lowest rate in 2016 and highest rate in 2018), with the annual rate of single-substance ED visits ranging from 2,017 to 2,413 per 100,000 individuals. The utilization-adjusted rate of estimated ED visits involving an alcohol disorder, the lowest of the three substances, ranged from 2,225 to 2,327 per 100,000

individuals, and ranged from 1,775 to 1,843 per 100,000 individuals for single-substance ED visits.

National Inpatient Sample

NIS is the largest publicly available all-payer inpatient administrative healthcare database in the United States, sponsored by AHRQ. NIS is a sample of discharges from participating community hospitals, reporting from 46 to 48 states and the District of Columbia per year. NIS data include ~7 million inpatient stays annually (unweighted), accounting for annual estimates of 35 million hospitalizations nationally after weighting (AHRQ, 2021, 2022b). In this evaluation, alcohol, marijuana, and cocaine data were compared.

Based on NIS data, from 2016 to 2020, alcohol-related disorder had the highest estimated annual number of hospitalizations, which was stable at ~1.8 million each year, with ~1.2 to 1.25 million estimated annual hospitalizations that involved alcohol-related disorder per year for single-substance alcohol. Marijuana-related disorder had the second-highest estimated annual number of hospitalizations, increasing from 795,140 in 2016 to 914,810 in 2020, with estimated annual hospitalizations that involved marijuana-related disorder per year for single-substance marijuana increasing from 373,160 to 452,985. The lowest estimated annual number of hospitalizations among these three substances was related to cocaine-related disorder, which ranged from 387,385 to 453,955 from 2016 to 2020, with estimated annual hospitalizations per year for single-substance cocaine increasing from 94,695 to 112,725, with the highest rates observed in 2018.

A utilization-adjusted rate of estimated hospitalizations was then calculated by dividing estimated annual number of hospitalizations for each substance as reported in NIS by the number of individuals reporting any past-year use of that substance as reported in NSDUH. The highest utilization-adjusted rate of estimated hospitalizations was observed for cocaine-related disorder, which ranged from 2016 to 2020 from 7,185 to 8,211 per 100,000 individuals with any past-year use, with the annual rate of single-substance hospitalizations ranging from 1,796 to 2,039 per 100,000 individuals. Marijuana-related disorder had the second-highest utilization-adjusted rate of estimated hospitalizations from 2016 to 2020, where the rates for marijuana related disorder ranging from 1,850 to 2,117 per 100,000 individuals, with the annual rate of single-substance hospitalizations ranging from 906 to 1,026 per 100,000 individuals. The utilization-adjusted rate of estimated hospitalizations involving an alcohol-related disorder was the lowest of the three substances, ranging from 987 to 1,039 per 100,000 individuals and ranging from 675 to 715 per 100,000 individuals for single-substance hospitalizations.

National Forensic Laboratory Information System

The National Forensic Laboratory Information System (NFLIS) is a program of the Diversion Control Division of DEA. Data from the NFLIS-Drug system serves as a surveillance resource to monitor drug encounters by law enforcement across the United States (Drug Enforcement Administration). Specifically, the NFLIS-Drug system collects data on drugs seized by law enforcement during a law enforcement investigation, and which are submitted to federal, state, and local forensic laboratories for analysis. Data fields include but are not limited to number of

“reports or exhibits” submitted to the laboratories, number of cases encompassing the exhibits, approximate dates of encounters, approximate location (states) of drug encounters and other drugs found in the encounters. The degree to which these and other fields are completed is dependent upon the individual laboratories.

As indicated above, NFLIS provides data on the number of “reports” or “exhibits,” consisting of drug evidence (e.g., bulk substance, cannabis resin) obtained during a law enforcement investigation (i.e., a drug “case”) that was sent and analyzed by federal, state, and local forensic laboratories. State and local forensic laboratories, and to a certain extent federal laboratories, primarily conduct qualitative analysis of drug exhibits and to a lesser extent quantitative analysis, depending upon goals and requirements of each case.

In NFLIS, a case may result in one or more reports or exhibits and that each exhibit may contain one drug or multiple drugs. Multiple drug exhibits (e.g., reports in combination) may represent exhibits in which drugs are mixed (e.g., mixed powder material) or in which drugs were found separately (e.g., individual drugs packaged separately but found in the same container). When reporting at the case level-data, all drugs identified in a drug-related incident are counted, although a small number of laboratories may choose to assign a single case number to all drugs related to an entire case.

Limitations on the NFLIS-Drug data, as noted by DEA, include that not all drugs encountered by law enforcement are sent for analysis and not all drugs sent to reporting forensic laboratories are tested. Seized drug evidence may not be sent for analysis or some forensic laboratories may have policies to not test submitted samples in drug cases that are dismissed, result in a guilty plea or a plea bargain was reached before samples are submitted for analysis or before being analyzed by the forensic laboratories (Pitts et al., 2023).

Annually and semiannually DEA publishes NFLIS-Drug national report estimates to account for nonreporting laboratories, among other things.¹⁵ An analysis of 2021 national estimates (Drug Enforcement Administration, 2021) for cannabis/THC, as reported in the published literature in comparison to other drugs seizures, is discussed below.¹⁶ The analysis of national estimates data allow us to compare the number of reports by year and reporting trends. In calculating national and regional estimates the DEA uses the National Estimates Based on All Reports approach, which uses all NFLIS-Drug reporting laboratories.

In 2021, there were a total of 1,326,205 drug reports identified by State and local forensic laboratories in the United States. This estimate represents an increase of approximately 3% from the drug reports identified in 2020. Nationally, 61% of all drug reports in NFLIS were identified

¹⁵ Detailed description of methods used in preparing national estimates is provided in the 2017 NFLIS statistical methodology publication found at: <https://www.nflis.deadiversion.usdoj.gov/nflisdata/docs/NFLIS-2017-StatMethodology.pdf> (Last accessed July 2023)

¹⁶ This category includes the following substances: Cannabis, Cannabis (All plant material excluding intact plants), Cannabis oil (Concentrated liquid resin extract), Cannabis plant (Intact plant), Cannabis resin (Hashish), Cannabis seed, Cannabis Stems, Concentrated cannabis, Tetrahydrocannabinol (organic) and Tetrahydrocannabinol (THC)-Non-specific (Source: DEA’s Drug and Chemical Evaluation Section Office of Diversion at DEA)

as involving methamphetamine (406,200 reports or 31%), cannabis/THC (167,669 reports or 13%), cocaine (165,162 reports or 12%) or heroin (72,315 reports or 5%).

In 2021, there were 1,027,219 drug-specific cases submitted to and analyzed by state and local laboratories, representing a 2% increase from drug specific cases in 2020. It is noted that although the total NFLIS number of drug reports increased in 2021 from 2020, the total number of cases and drugs reported continues to be noticeably lower than the number reported for the years before the COVID-19 pandemic. Nationally, in 2021, 45% of all drug cases contained one or more reports of methamphetamine, followed by cocaine and cannabis/THC which were identified in 18% and 17% of all drug cases, respectively. Heroin was identified in 8% of all drug cases.

National trends indicate that the number of cannabis/THC reports as well as the number of cases in which cannabis/THC was identified decreased from 2015 through 2021. From 2020 to 2021 the number of cannabis/THC reports decreased from 188,735 to 167,669 (Drug Enforcement Administration). It should be noted that a decrease in the number of reports of cannabis/THC does not necessarily mean that there was a decrease in the number of cannabis/THC encounters, it means that there was a decrease in the number of exhibits submitted by law enforcement for analysis or a decrease in the number of exhibits processed (analyzed) by forensic laboratories.

Conclusions

The most notable conclusion from an evaluation of various epidemiological databases related to the medical outcomes from abuse of selected drugs is that for all measures that were evaluated from 2015 to 2020, the rank order of the comparators in terms of greatest adverse consequence typically places alcohol, heroin, and/or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking. This pattern was also observed for PC data with regard to serious medical outcomes, including death, where marijuana was in the lowest ranking group. This demonstrates that there is consistency across databases, across substances, and over time, and although abuse of marijuana produces clear evidence of harmful consequences, including substance use disorder, they are relatively less common and less harmful than some other comparator drugs. Additionally, the number of law enforcement encounters with marijuana decreased from 2020 to 2021, at a time when law enforcement encounters were increasing for other scheduled drugs of abuse. However, as noted above in Factor 1a, there are limitations in comparing descriptive data on adverse outcomes across drugs.

FACTOR 6. WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

Under the sixth factor, the Secretary must consider the risks posed to the public health by marijuana. Previous factors have provided data that contribute to an understanding of this issue. For example, Factor 2 includes a discussion of the typical psychological, behavioral, and physiological effects of marijuana that may impact public health. Factor 4 details the abuse patterns and trends of marijuana use that can affect public health, using data from NSDUH, BRFSS, RADARS-NMURx, MTF, YRBSS, and ICPS. Factor 5 includes a discussion of the risk

to the public health as measured by data from NPDS, NSDUH, TEDS, NAVIPPRO, NEDS, and NIS.

Factor 6 addresses which sectors of the public are most at risk by detailing NSDUH data related to the demographics of United States individuals meeting criteria for marijuana use disorder, TEDS data related to the demographics of admission to treatment centers for marijuana use disorder, NEDS and NIS data on admissions to EDs and hospitals related to a marijuana poisoning, ToxIC Core Registry for intentional and unintentional exposure, and NPDS data describing the risks to youth of unintentional exposure to marijuana. The risks to public health are also detailed through NSDUH data on driving under the influence of marijuana in adults and high school students. Finally, data are provided regarding the risk of serious AEs and death associated with nonmedical use/use of uncertain intent of marijuana as reported to FAERS, CAERS, NVSS-M, DIM, DAWN, FDA's Sentinel Distributed Database System, and CMS.

This review uses sources of data on overdose, healthcare encounters for poisoning, and AEs that do not specify whether the person affected was using marijuana or any of the comparator substances for medical or nonmedical reasons. As a result, overdose death, healthcare encounters for poisoning, and spontaneously reported AEs involving marijuana or other substances are described as "use of uncertain intent" when the intent of use cannot be determined.

Epidemiology of Risk Posed by Marijuana to Public Health

Demographics of Marijuana Use Disorder

NSDUH data from 2021 show that among those individuals with past-year, marijuana nonmedical-only use, the prevalence of meeting criteria for marijuana use disorder is highest for those who are age 12-17 years (44%), even among individuals who used only marijuana for nonmedical reasons (37%). The data also show that as age increases, the prevalence of marijuana use disorder coinciding with nonmedical use of marijuana decreases in a linear fashion, depending on whether nonmedical marijuana use is examined overall or as a single substance: age 18-25 years (39% and 29%, respectively), age 26-34 years (35% and 26%, respectively), age 35-64 years (23% and 20%), and age 65 years or older (13% and 11%). These data suggest that the likelihood of being diagnosed with marijuana use disorder is higher if the individual might have been using other drugs nonmedically in addition to marijuana, compared to only using marijuana for nonmedical reasons.

TEDS admission data from 2020 show that there were 139,481 admissions for substance use disorder treatment where marijuana was the primary drug for admission, which represents 10% of 1.4 million total admissions. Of these admissions for marijuana as the primary drug of admission, 69% of patients were male. An age analysis of the admissions where marijuana was the primary drug for admission shows that the age groups accounting for the highest proportion of admission were ages 35 to 64 years (25%) and 18 to 24 years (24%), followed by the groups for ages 25-29 years (19%), 12 to 17 years (17%), and 30 to 34 years (15%). There were very few admissions for those ages 65 years or older (less than 1%). When a further analysis of the treatment admissions for youth (the 12-17 age group) was conducted compared to other drugs,

the primary drug of admission was marijuana/hashish for the vast majority of admissions (69%), with alcohol as the second most frequent primary drug of admission (9%). The comparator drugs heroin, cocaine, and benzodiazepines were each the primary drug of admission in ~1% of admissions, with the category of “other drugs” as primary drug of admission accounting for 6% of admissions. A primary drug of admission was not reported in 13% of admissions.

Risk of ED Visit and Hospitalization from Marijuana Poisonings

Data from the NEDS and NIS databases for 2016 to 2020 show that marijuana poisonings in the United States resulted in ED visits ranging from 29,050 to 49,357 visits per year and hospitalizations ranging from 12,940 to 18,470 per year. Although most ED visits involving marijuana poisoning were for marijuana as a single substance, most hospitalizations involving marijuana poisoning involved at least one additional substance.

When the NEDS database is evaluated for 2020 numbers of ED visits involving poisoning from a single substance, heroin had the highest number of cases (n = 18,440), followed by benzodiazepines (n = 10,427), marijuana (n = 7,880), alcohol (n = 5,035), and cocaine (n = 2,850). When utilization-adjusted rates of ED visits involving single-substance poisoning were calculated per 100,000 individuals who reported any past-year use in NSDUH in 2020, heroin had the highest rate (n = 8,661), followed by benzodiazepines (n = 961) and cocaine (n = 240). The lowest rates were reported for marijuana (n = 79) and alcohol (n = 10).

An evaluation of NEDS 2020 data regarding the reason for poisoning involved in an ED visit with each comparator shows that accidental/unintentional poisoning was the most frequently reported reason for cocaine (n=29,563), heroin (n=108,862), benzodiazepines (n=42,339), alcohol (n=25,791), and marijuana (n=32,914). However, for benzodiazepines, poisoning classified as adverse effects of the drug (n=27,404) was often reported, along with very high numbers also reported for intentional/self-harm (n=37,389). Also, for alcohol, intentional/self-harm was also reported at a relatively high number (n=7,808). For cocaine, heroin, and marijuana, poisonings classified as intentional/self-harm, assault, and undetermined intent occurred in fewer cases (n=less than 5,000 for each substance and respective intent).

When the NIS database is evaluated for 2020 estimated numbers of hospitalizations involving poisoning from a single substance, benzodiazepines had the highest estimated number of hospitalizations as a single substance (n=19,420), followed by alcohol (n=7,380), heroin (n=7,085), cocaine (n=7,065), and marijuana (n=5,240). When utilization-adjusted rates of hospitalizations involving single-substance poisoning were calculated per 100,000 individuals who reported any past-year use in NSDUH in 2020, heroin had the highest rate (757 hospitalizations per 100,000 individuals), followed by cocaine (145 hospitalizations per 100,000 individuals), and benzodiazepines (73 hospitalizations per 100,000 individuals). The lowest rates were reported for marijuana (11 hospitalizations per 100,000 individuals) and alcohol (4 hospitalizations per 100,000 individuals).

The disposition at discharge from hospitalization after single substance drug poisoning was also evaluated, showing that the largest estimated number of hospitalizations for each comparator were “routine” (discharge to home or self-care) for benzodiazepines (n=9,345), alcohol (n=5,020), cocaine (n=4,715), marijuana (n=4,315), and heroin (n=4,140). Transfers to skilled

nursing facility, intermediate care facility was the second most frequent discharge disposition for benzodiazepines (n=5,810) and alcohol (n=955), and the third most frequent discharge disposition for cocaine (n = 630). Discharge to home health care was the third most frequent discharge disposition for marijuana (n=270) and heroin (n=145). Those cases where the individual left the hospital against medical advice were small for benzodiazepines (n = 580) and alcohol (n=690) but were the second most frequent discharge disposition for heroin (n=1,445), cocaine (n=695), and marijuana (n=365). For hospitalizations involving poisoning as a single substance that resulted in death at discharge, the largest numbers were from heroin (n=590) and cocaine (n=550), with smaller numbers for benzodiazepines (n=365) and alcohol (n=135). The number for marijuana could not be calculated because statistics representing fewer than 10 hospitalizations were suppressed. When utilization-adjusted rates per 100,000 individuals who reported any past-year use in NSDUH in 2020 were calculated for hospitalizations involving poisoning as a single substance that resulted in deaths, the highest rates were from heroin (63 hospitalizations per 100,000 individuals) and cocaine (11 hospitalizations per 100,000 individuals), with very small numbers for benzodiazepines (1 hospitalizations per 100,000 individuals) and alcohol (n=less than 1 hospitalizations per 100,000 individuals). Utilization-adjusted rates per 100,000 individuals who reported any past-year use in NSDUH in 2020 could not be calculated for marijuana because statistics representing fewer than 10 hospitalizations were suppressed.

Toxicology Investigators Consortium Core Registry

The ToxIC Core Registry comprises over 50 locations throughout the United States, with several international locations also participating. The majority of active United States medical toxicology practices and accredited medical toxicology fellowship programs are participating locations. All cases entered into the ToxIC Core Registry represent a patient that has been formally evaluated and treated by a medical toxicology physician as part of their medical care at a participating center (American College of Medical Toxicology).

A search of the ToxIC Core Registry from January 1, 2012, to July 31, 2022, yielded 829 single-substance, marijuana-containing product exposure cases. The majority of cases involved individuals ages 19 to 65 (n=277) or 6 years and younger (n=277). Intentional ingestion was described in 427 cases, of which 290 involved misuse/abuse, 17 cases involved therapeutic intent, and 120 cases had no additional information. Unintentional ingestion was described in 342 cases, of which 309 cases were in children aged 13 years or younger.

From the 829 marijuana cases in the ToxIC Core Registry, 575 involved acute exposure and 145 involved chronic exposure. A majority of cases in the ToxIC Core Registry had no major/notable vital sign abnormalities (n=552 (67%)); the most frequently reported vital sign abnormality was tachycardia (n=103). Furthermore, a majority of cases in the ToxIC Core Registry exhibited no toxidrome (n=511 (62%)), whereas the most frequently reported toxidrome was sedative-hypnotic (n=105). Of the 829 marijuana cases, 499 (60%) resulted in admission to a hospital; of the 499 hospital admissions, 202 (40%) were admitted to a critical care unit. An additional 320 cases received medical care in an ED or observation unit and were not hospitalized. Notably, ToxIC Core Registry cases represent patients who were formally evaluated and treated by a medical toxicology physician as part of their care at a participating

medical center. It is possible that patients who had formal toxicologist consultation had a more complicated or severe clinical presentation following cannabis ingestion than usually expected, which could contribute to the high rate of hospital and critical care unit admissions among ToxIC Core Registry cases.

The ToxIC Core Registry had two cases involving marijuana-containing product exposure with an outcome of death. Both fatal cases involved the inhalational route of exposure to a non-pharmaceutical product (a substance other than an approved medication) in the setting of intentional misuse/abuse. One of the two deaths involved acute exposure in a 16-year-old boy who had life support withdrawn. The other death involved chronic exposure in a 21-year-old man with vaping-induced pulmonary injury.

Risks from Unintentional-General Exposure to Marijuana

NPDS data provide information about unintentional-general exposures to a drug, out of the total number of PC cases for that drug during the period of 2015 to 2021. NPDS states that most unintentional exposures in children should be coded as “unintentional-general” (e.g., a child obtaining a drug from a grandparent’s prescription bottle). The highest numbers of unintentional-general exposure cases in relation to total PC cases were for benzodiazepines (n=40,085 out of 440,030) and alcohol (n=22,350 out of 370,118). Marijuana had the third highest number of unintentional-general exposure cases (n=15,301 out of 63,645), with all other comparator cases documenting fewer unintentional-general exposures (hydrocodone (n=10,455 out of 106,934), oxycodone (n=9,769 out of 99,534), tramadol (n=8,453 out of 67,582), zolpidem (n=5,604 out of 71,575), cocaine (n=1,298 out of 37,538), heroin (n=1,066 out of 52,713), illicit fentanyl (n=186 out of 5,085), and ketamine (n=106 out of 2,096)).

When a utilization-adjusted rate for 2021 was calculated by dividing the unintentional-general exposure case data from NPDS by the number of individuals ages 12 years and older with any past-year use from NSDUH, the highest rates of unintentional-general exposure per one million people were observed for benzodiazepines (rate=146 cases per one million people with any past-year use) and heroin (rate=127 cases per one million people with any past-year use), followed by marijuana (rate=98 cases per one million people with any past-year use), zolpidem (rate=66 cases per one million people with any past-year use), ketamine (rate=59 cases per one million people with any past-year use), cocaine (rate=52 cases per one million people with any past-year use), oxycodone (rate=52 cases per one million people with any past-year use), tramadol (rate=46 cases per one million people with any past-year use), hydrocodone (rate=25 cases per one million people with any past-year use), and alcohol (rate=18 cases per one million people with any past-year use).

Marijuana had the highest percent of PC unintentional-general exposure cases as a single substance (92%). Oxycodone, alcohol, hydrocodone, tramadol, zolpidem, and benzodiazepines ranged from 72-76% as the percent of unintentional-general exposure cases to that drug as a single substance, while heroin, fentanyl, ketamine, and cocaine ranged from 54-68% as the percent of unintentional-general exposure cases to that drug as a single substance.

The number of unintentional-general cases in children ≤ 12 years was greater for marijuana (n=12,757) than for most comparator substances (n=27 to 7,731), apart from alcohol (n=14,753) and benzodiazepines (n=30,021). A similar pattern was observed for children < 6 years where the number of unintentional-general cases was greater for marijuana (n=10,636) than for most comparator substances (n=25 to 7,499), apart from alcohol (n=13,971) and benzodiazepines (n=28,962).

Among single-substance unintentional-general exposure cases, ingestion was the predominant exposure route for children 6 years of age or younger, as well as for children aged 6 to 12 years, for marijuana (93% to 97%) and for the other comparators with at least 10 cases (65 to 100%).

Among United States PC cases from 2015 to 2021 involving unintentional-general exposure to marijuana as a single substance by children under 6 years old, the most frequently documented related clinical effects, based on severity, timing, and assessment of clinical effects, were CNS depression (mild/moderate) (82%), vomiting (10%), and tachycardia (10%).

Finally, the ToxIC Core Registry contains cases of unintentional exposure to marijuana-containing products in pediatric patients. Of the 829 ToxIC Core Registry cases involving single-substance, marijuana-containing product exposure with uncertain intent, 342 (41%) involved unintentional ingestion. Of the 342 cases of unintentional ingestion, 309 (90%) were in pediatric patients less than 13 years of age.

Risk of Driving Under the Influence of a Drug

NSDUH data from 2021 were examined to evaluate the prevalence of reported driving under the influence of marijuana, alcohol, cocaine, or heroin over the past year in individuals ages 16 years and older. The prevalence of driving under the influence of a drug when all individuals over the age of 16 are combined was 4% for marijuana and 5% for alcohol, with less than 1% for cocaine and for heroin.

When the NSDUH data are evaluated by age cohorts, the highest prevalence for driving under the influence of marijuana was in individuals who were age 21 to 25 (10%), followed by individuals aged 26-34 (7%), aged 16 to 20 (6%), aged 35 to 64 (3%) and aged 65 and older (1%). An age cohort analysis for alcohol showed the highest prevalence for driving under the influence in individuals aged 21 to 25 (8%), followed by individuals aged 26 to 34 (7%), aged 35 to 64 (6%) and ages 16 to 20 and 65 and older (both 3%).

Additional information about driving under the influence is provided by the YRBSS, which provided data on high school students, aged 16 years and older in 2017 (the year for which comparative data for marijuana and alcohol were available). Among individuals who reported driving in the past month and who also reported using marijuana in the past month, 53% reported driving under the influence of marijuana at least once, 21% of whom did so at least six times in the past month. In contrast, among individuals who reported driving in the past month and who also reported using alcohol in the past month, 16% reported driving under the influence of alcohol.

Adverse Events Associated with Marijuana Use Reported to FDA

FAERS is a database that contains adverse event reports, medication error reports, and product quality complaints submitted to FDA and is designed to support FDA's postmarket safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation (US Food and Drug Administration). The CAERS database contains information on adverse event and product complaint reports submitted to FDA for foods, dietary supplements, and cosmetics (US Food and Drug Administration). Separate from their purpose of supporting the safety of FDA-regulated products, the FAERS and CAERS databases contain voluntary reports involving unapproved products (e.g., marijuana) submitted to FDA directly from healthcare professionals, consumers, and other reporters. FDA does not require that a causal relationship between a product and event be proven; furthermore, reports do not always contain adequate information to assess the causal relationship between an event and a drug/substance. Because FDA does not receive reports for every adverse event or medication error that occurs with a product, FAERS/CAERS data cannot be used to calculate the incidence of an adverse event or medication error in the United States population.

A search of the FAERS and CAERS databases from January 1, 2012, to October 31, 2022, yielded 133 cases describing AEs or quality/labeling complaints involving marijuana-containing products directly reported to FDA. An additional 11 cases had an outcome of death and listed a marijuana-containing product; of these 11 death cases, 2 were attributed to another cause, 8 had insufficient information to assess the causal role of marijuana, and 1 case narrative did not describe an outcome of death (i.e., was likely miscoded). Therefore, the 11 fatal cases were not included in the separate analysis of the 133 cases involving a marijuana-containing product.

From 2012 to 2018, fewer than 10 cases per year involving marijuana were reported to FDA's FAERS/CAERS databases; similarly, in 2020, 2021, and the first 10 months of 2022, between 10 and 20 cases involving marijuana were reported each year. However, in 2019, FDA received 66 cases involving marijuana-containing products; of the 66, a total of 61 involved vape products. Notably, of 84 total cases involving vape products, 61 were received in 2019. The majority of marijuana cases (n=103) involved individuals who were ages 19 to 65 years (n=78) or 13 to 18 years (n=25).

Of 133 marijuana cases in FAERS and CAERS, 92 had one or more serious outcomes, including: hospitalization (n=54), life-threatening (n=28), required medical intervention (n=21), disability (n=15), or other serious outcome (n=35); in addition to the 54 hospitalizations, 17 cases described an ED visit.

Of the 133 marijuana cases in FAERS and CAERS, 127 described an adverse event; 10 or more of these 127 cases were coded with terms describing the following events: difficulty breathing (n=29), cough (n=14), nausea (n=14), seizure (n=13), fever (n=11), chest pain (n=10), loss of consciousness (n=10), respiratory disorder (n=10), and vomiting (n=10).

National Vital Statistics System-Mortality and Drug-Involved Mortality

NVSS-M contains information on United States death certificates that contain a single, underlying cause of death, up to twenty multiple causes, and demographic data. The underlying cause of death indicated the injury intent (e.g., accident, suicide, undetermined) and whether the cause was drug-induced (CDC, 2021c). DIM data consist of NVSS-M data linked to the literal-text fields in the death certificate containing information written by the official certifying the death, including the cause of death, manner, and circumstances. Any drug mentioned in a literal text field is assumed to be involved in the death unless contextual information indicates otherwise (CDC, 2018). DIM data provide information about drug-involved mortality at the level of the active ingredient such that the selected comparators could be evaluated, but the data have not recently been updated.

Over a 10-year period (2012 to 2021) the total number of overdose deaths involving marijuana was much lower than that of most comparators. Fentanyl had the highest total number of overdose deaths (n=258,785) followed by cocaine (n=119,208), heroin (n=118,992), and benzodiazepines (87,581). Alcohol had a much lower number of overdose deaths (n=10,484), with marijuana producing the lowest number of overdose deaths (n=5,957). Polysubstance deaths were common. Overall, 5% or less of overdose deaths involving marijuana and most comparators documented were single substance, with the exception of alcohol (13%).

A slightly different rank order of the comparators was seen when overdose deaths in NVSS-M were evaluated in the same period for single substances: fentanyl had the highest total number of overdose deaths, as a single substance (n=12,843), followed by those for heroin (n=6,078), cocaine (n=2,774), alcohol (n=1,338), and benzodiazepines (n=277), with marijuana producing the lowest number of overdose deaths as a single substance (n=160). When utilization-adjusted single-substance overdose death rates were calculated per 100,000 individuals who reported any past-year use in NSDUH in 2020 (the most recent year for which data on marijuana as a single substance in NVSS-M were not suppressed due to small death counts), the drug with the highest rate is heroin (22.22 deaths per 100,000 people who reported past-year use), followed by cocaine (4.79 deaths per 100,000 people who reported past-year use). The utilization-adjusted single-substance overdose death rates were especially low for benzodiazepines (0.14 deaths per 100,000 people who reported past-year use) and alcohol (0.08 deaths per 100,000 people who reported past-year use), with marijuana producing the lowest rate (0.04 deaths per 100,000 people who reported past-year use). Utilization-adjusted estimates of illicit fentanyl use were not available as past-year use of illicit fentanyl is not captured by NSDUH.

When DIM data from 2017 (the latest year for which data are available for comparators) are evaluated as total overdose deaths and as single-substance overdose deaths, as mentioned in the death certificate literal text as contributing to the death, fentanyl had the highest number of total and single substance overdose deaths (n=27,028 and 6,057, respectively), followed by heroin (n=15,831 and 2,660, respectively) cocaine (n=14,796 and 2,987), and benzodiazepine (n=10,375 and 512, respectively). Oxycodone (n=5,386 and 695, respectively), hydrocodone (n=2,588 and 275, respectively), and tramadol (n=1,078 and 120, respectively) had the next highest total and single substance overdose deaths reported, with zolpidem (n=434 and 13, respectively), marijuana (n=202 and 12, respectively), and ketamine (n=69 and 7, respectively)

showing the lowest rates of overdose deaths. When utilization-adjusted total overdose death rates were calculated for total single substance overdose deaths per 100,000 individuals who reported any past-year use in NSDUH in 2017, heroin had the highest rate (1733 per 100,000 individuals), followed by cocaine (249 per 100,000 individuals), benzodiazepines (179 per 100,000 individuals), oxycodone (142 per 100,000 individuals), tramadol (63 per 100,000 individuals), zolpidem (48 per 100,000 individuals), and hydrocodone (42 per 100,000 individuals). Marijuana had the lowest utilization-adjusted rate (0.5 per 100,000 individuals).

Drug Abuse Warning Network Surveillance System

DAWN is a public health surveillance system administered by SAMHSA that provides nationally representative estimates on ED visits related to recent substance use and misuse by reviewing all electronic health records from the EDs of non-federal, short-stay, general surgical and medical hospitals located in the United States. DAWN uses a hybrid design of sentinel hospital-based surveillance (i.e., large urban hospitals located in counties with high counts and rates of morbidity and mortality due to opioid, cocaine, and stimulant overdose) and probability sample-based surveillance (stratified random sampling method) to select a sample of 53 hospitals as well as a non-probability sample of 13 hospitals that were located in areas highly affected by drug overdoses (SAMHSA, 2022a).

An evaluation of the 2021 estimated number of ED visits in DAWN where the specific drug was a direct cause (e.g., overdose) or a contributing factor (e.g., injury) show a wide range of ED visits between comparator drugs, where alcohol (n = 2,996,516) represents the greatest estimated number of ED visits, followed to a much lesser degree by marijuana (n = 804,285), heroin (n = 506,355), cocaine (n = 342,770), and fentanyl (n = 123,563). The utilization-adjusted rate of 2021 ED visits in DAWN per 100,000 individuals who reported any past-year use in NSDUH in 2020 also show a different rank order between the comparators, where heroin (46,281 ED visits per 100,000 people who reported past-year use) represents the highest rate, followed to a much lesser degree by cocaine (7,119 ED visits per 100,000 people who reported past-year use) and alcohol (1,715 ED visits per 100,000 people who reported past-year use), with marijuana (1,529 ED visits per 100,000 people who reported past-year use) showing the lowest rate. Data for any past-year use of illicit fentanyl were not available in NSDUH.

When an age evaluation was conducted on DAWN data for all ED visits in 2020, the largest estimated total number and percentage of ED visits were reported for individuals aged 26-44 years for all comparators, where alcohol (n=1,213,589; 41%) had the highest numbers, followed to a much lesser degree by marijuana (n=362,250; 45%), heroin (n=290,293; 57%), cocaine (n = 155,858; 46%), and fentanyl (n=77,375; 63%). The total number and percentage of ED visits was second highest for individuals aged 45-64 years for three comparators: alcohol (n=1,168,342; 39%), heroin (n=152,160; 30%), cocaine (n=132,892; 39%), while this age group was third highest for marijuana (n=132,305; 17%) and fentanyl (n=18,127; 15%). For individuals aged 18 -25, this age group was second highest for total number and percentage of ED visits for marijuana (n=215,307; 27%) and fentanyl (n=20,722; 17%) and third highest for alcohol (n=299,951; 10%), heroin (n=40,964; 8%), cocaine (n=32,974; 10%). After adjusting for the U.S. resident population in each age group, the 18- to 25-year-old age group had the highest estimated rate of ED visits involving marijuana (626 ED visits, per 100,000 U.S. resident

population). For each comparator, the population-adjusted rate of ED visits was highest among 26- to 44-year-olds.

When an analysis was conducted on ED visits from the 13 participating hospitals from areas highly affected by drug overdoses between March to December 2021, the highest number of ED visits involved alcohol (n=31,458), with lower numbers for ED visits involving marijuana (n=6,368), cocaine (n=5,440), heroin (n=3,499), and fentanyl (n=3,064). When the proportion of these ED visits were calculated on the basis of single substance (i.e., visits in which the medical record documented only that substance as involved in the adverse event), the proportion was highest for alcohol (78%), followed by heroin (44%), with similar proportions for fentanyl (38%), marijuana (37%), and cocaine (35%).

FDA's Sentinel Distributed Database System

FDA's Sentinel System is an active surveillance system for post-marketing medical product safety that uses administrative claims data from three national health insurers (Aetna, Humana Inc., and Optum) and six regional integrated delivery systems (Health Partners, Kaiser Permanente Colorado, Kaiser Permanente Hawaii, Kaiser Permanente Northwest, Kaiser Permanente Washington, and Marshfield) that contribute to the Sentinel Distributed Database (FDA, 2023a, 2023b, 2023c, 2023d). Administrative billing ICD-10-CM codes as a result of healthcare encounters (inpatient, outpatient/ED visit, or institutional stay) that documented poisoning involving marijuana, cocaine, alcohol, heroin, or benzodiazepines were used for the evaluation.

From April 2016 to June 2022, the greatest number of healthcare encounters (i.e., inpatient, outpatient, ED, or institutional) in the Sentinel Distributed Database were for benzodiazepine poisonings that involved 63,074 encounters in a total of 39,864 unique patients (1.6 encounters per individual). The next highest number of healthcare encounters were 25,272 encounters involving heroin poisonings in a total of 15,707 unique patients (1.6 encounters per individual), 17,961 encounters involving marijuana poisonings in a total of 14,668 unique individuals, representing 1.2 encounters per individual, 15,599 encounters involving alcohol poisonings in a total of 11,891 unique individuals (1.3 encounters per individual), and 9,062 encounters involving cocaine poisonings in a total of 6,382 unique individuals (1.4 encounters per individual).

The Sentinel Distributed Database shows that for encounters involving marijuana poisonings, the mean age of the individuals was 35 years and 53% were male. Individuals with encounters involving marijuana poisoning often had prior encounters with diagnoses of chronic pain (30%), anxiety disorders (27%), depression (20%), nausea (20%), hypertension (17%), marijuana-related disorders (14%), alcohol-related disorders (6%), and opioid-related disorders (5%).

For encounters involving heroin poisonings, the mean age of the individuals was 35 years and 68% were male. Individuals with encounters involving heroin poisonings frequently had prior encounters with a diagnosis of nicotine use/vaping (43%), opioid-related disorders (47%), alcohol-related disorders (20%), marijuana-related disorders (18%), and cocaine-related disorders (15%) as well as of depression (32%), chronic pain (34%), and sleep disorders (18%).

For encounters involving alcohol poisonings, the mean age of the individuals was 40 years and 53% were male. Individuals with encounters involving alcohol poisoning frequently had prior encounters with a diagnosis of anxiety disorder (40%), chronic liver disease (10%), depression (38%), hypertension (28%), nicotine/vaping use (30%), sleep disorders (19%), alcohol-related disorders (37%), marijuana-related disorders (6%), and opioid-related disorders (8%).

For benzodiazepine encounters, the mean age of the individuals was 42 years and, 62% were female. Individuals with encounters involving benzodiazepine poisonings frequently had prior encounters with a diagnosis of chronic pain (48%), anxiety disorders (61%), depression (50%), hypertension (32%), sleep disorders (30%), alcohol-related disorders (15%), and opioid-related disorders (14%).

For cocaine encounters, the mean age was 40 years and 70% were male. Individuals with encounters involving cocaine poisonings had evidence of prior encounters with a diagnosis of nicotine use/vaping (39%), cocaine-related disorders (24%), opioid-related disorders (20%), alcohol-related disorders (19%), marijuana-related disorders (12%) as well as of depression (29%), chronic pain (38%), and sleep disorders (20%).

Individuals with encounters involving marijuana poisoning were slightly younger than those with encounters involving cocaine, alcohol, or benzodiazepine poisoning and similar in age to those with encounters involving heroin poisoning. They appeared to be less likely than individuals with encounters for poisonings involving the selected federally controlled substances or alcohol to have a diagnosis in the 6 months prior to the index event for certain psychiatric conditions (anxiety, depression, psychotic disorders, PTSD, sleep disorders), and non-acute pain. They also were less likely than individuals with encounters for poisonings involving the selected federally controlled substances or alcohol to have a diagnosis of nicotine use/vaping. However, the relatively low frequency of chronic respiratory diseases in this group might represent a biased underestimate of nicotine use/vaping, since tobacco use, which is generally not well captured in claims data, is even less likely to be captured among patients who do not have respiratory diseases. Other substance-related disorders, except for marijuana-related disorders, were also less common among individuals with encounters involving marijuana poisoning than for those with encounters for poisonings involving the selected federally controlled substances or alcohol.

CMS Medicare

Medicare is a national health insurance program administered by the CMS that provides healthcare coverage for people aged 65 years or older, as well as those who qualify because of a disability and/or end-stage renal disease (ESRD) regardless of age (CMS, 2021, 2023). The study populations were comprised of beneficiaries with continuous enrollment in Medicare Fee-For-Service (FFS) or Medicare Advantage (MA) in the 183 days prior to the first day of each calendar year and through the full calendar year or through the date of death (if they died during that year). The populations did not include beneficiaries residing in a nursing home for more than 100 days and those ages 18-64 years with ESRD in the 183 days prior to the index date. Billing codes from the ICD-10-CM were used to define the outcomes of interest as the first calendar-year occurrence of a given medical encounter (outpatient/professional services, ED

visit, or hospitalizations) related to poisoning by or adverse effect of marijuana, cocaine, alcohol, heroin, or benzodiazepines. The main measure of interest was the rate of medical encounters involving poisonings in the relevant study population for a given calendar year.

The study included a total of 63,161,236 unique beneficiaries of Medicare FFS or MA during 2017 to 2021. A total of 26,214 (0.04%) FFS or MA beneficiaries had one or more encounters involving marijuana poisoning, 22,071 (0.03%) had one or more encounters involving cocaine poisoning, 25,657 (0.04%) had one or more encounters involving alcohol poisoning, 201,772 (0.32%) had one or more encounters involving benzodiazepine poisoning, and 36,454 (0.06%) had one or more encounters involving heroin poisoning.

Over half (53.6%) of healthcare encounters involving marijuana poisonings among Medicare FFS beneficiaries and nearly half (47.1%) of such encounters among Medicare MA beneficiaries occurred in individuals ages <65 years. As such, the mean age of Medicare beneficiaries with healthcare encounters involving marijuana poisonings was younger than the overall Medicare population (mean age (SD): 58.8 (16.6) years vs 69.7 (11.8) years in FFS; mean age (SD): 62.3 (14.0) years vs 70.2 (10.2) years in MA). The proportion of African American/Black race was higher among Medicare beneficiaries with healthcare encounters involving marijuana poisonings than among the overall Medicare population (14.7% vs 9.1% in FFS; 19.1% vs 13.0% in MA), as was the proportion of low-income beneficiaries enrolled in both Medicare and Medicaid (46.8% vs 17.6% in FFS; 42.9% vs 20.2% in MA). Also, among Medicare beneficiaries with healthcare encounters involving marijuana poisonings, certain psychiatric and chronic medical conditions were noted in the 6-month period before the encounter of interest to a greater extent than among the overall Medicare population; these conditions included opioid-, nicotine-, alcohol-, marijuana-, and cocaine-related disorders as well as opioid, marijuana, and benzodiazepine poisonings.

Beneficiaries with healthcare encounters involving marijuana poisonings had a similar age as those with alcohol poisonings, were younger than those with benzodiazepine poisonings, and older than those with cocaine and heroin poisonings. Beneficiaries with healthcare encounters involving cocaine and heroin poisonings had a higher proportion of documented cases of opioid, nicotine, alcohol, cocaine, and other substance-related disorders than those with encounters involving marijuana poisonings.

Annual rates per 100,000 beneficiaries of healthcare encounters involving marijuana poisonings in the population ages ≥ 65 years were very low, with the highest rate (7.2 per 100,000 beneficiaries) in 2019 and 2021; for disabled beneficiaries ages <65 years, the highest rate (46.7 per 100,000 beneficiaries) was recorded in 2019.

Annual rates per 100,000 beneficiaries of healthcare encounters involving cocaine poisonings were also very low and ranged from 2.3 to 3.7 per 100,000 beneficiaries ages ≥ 65 years from 2017 to 2021, respectively. For disabled beneficiaries ages <65 years, rates of encounters involving cocaine poisonings appear to follow a downward trend, ranging from 55.7 to 51.5 per 100,000 beneficiaries, with the lowest rate (47.8 per 100,000) in 2020.

Annual rates per 100,000 beneficiaries of healthcare encounters involving alcohol poisonings were also in the same range as rates of marijuana and cocaine poisoning encounters for each of the two populations, with a suggestion of downward trend. During the 2017–2021 study period, rates of alcohol poisoning encounters among beneficiaries ages ≥ 65 years went from 6.8 to 5.4 per 100,000 beneficiaries while rates for the disabled population ages < 65 years ranged from 55.4 to 30.6 per 100,000 beneficiaries.

Similarly, in the disabled population ages < 65 years, annual rates per 100,000 beneficiaries for heroin poisoning encounters showed a downward trend with 115.6 per 100,000 beneficiaries in 2017 and 90.8 per 100,000 in 2021; rates among beneficiaries ages ≥ 65 years ranged from 3.9 to 5.4 per 100,000 beneficiaries.

Finally, annual rates per 100,000 beneficiaries of healthcare encounters for benzodiazepine poisonings showed a substantial decreasing trend with rates going from 71.7 to 46.2 per 100,000 beneficiaries ages ≥ 65 years and from 349.3 to 200.8 per 100,000 beneficiaries in the disabled population ages < 65 years.

Conclusions

The risks to the public health posed by marijuana are low compared to other drugs of abuse (e.g., heroin, cocaine, benzodiazepines), based on an evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and most importantly, for overdose deaths. The rank order of the comparators in terms of greatest adverse consequences typically places heroin, benzodiazepines and/or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking, especially when a utilization adjustment is calculated. For overdose deaths, marijuana is always in the lowest rankings among comparator drugs. These evaluations demonstrate that there is consistency across databases, across substances, and over time and that although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs. However, as noted above in Factor 1a, there are limitations in comparing descriptive data on adverse outcomes across drugs.

FACTOR 7. ITS PSYCHIC OR PHYSIOLOGIC DEPENDENCE LIABILITY

Under the seventh factor, the Secretary must consider the psychic or physiologic dependence liability of marijuana.

Psychic Dependence

The term “psychic or psychological dependence” has been used to convey a similar state to that of addiction (O'Brien, 1996). For diagnosis purposes, the DSM-V has combined “abuse” and “drug dependence” (i.e., addiction) previously specified in the DSM’s Fourth Edition into a single “substance use disorder,” which may occur in a broad range of severity, from mild to severe (Hasin et al., 2013).

The abuse potential of a drug can be assessed, in part, by evaluating the rewarding effects produced by that drug in humans and animals (Rastegar & Fingerhood, 2020). As described in Factor 2, rodent behavioral studies show that $\Delta 9$ -THC (the primary compound in marijuana that is responsible for its abuse potential) produces both self-administration and conditioned place preference. These results demonstrate that $\Delta 9$ -THC has rewarding properties that are indicative of abuse potential. As described in Factor 5, there is ample epidemiological evidence that marijuana is self-administered by humans because of its ability to produce rewarding psychological effects, such as euphoria.

In some individuals, extensive use of marijuana can lead to a substance use disorder. In the DSM-5, Cannabis Use Disorder (CUD) shares diagnostic criteria common to substance use disorders for other drugs of abuse. In general, substance use disorders listed in the DSM-5 are defined by an inability to cease drug use despite harmful consequences (American Psychiatric Association, 2013; Connor et al., 2021). Estimates of CUD in regular individuals who use marijuana vary and range from about 10-20% (Connor et al., 2021; Leung et al., 2020). This is similar to data from the United States National Comorbidity Study, which showed that 9% of lifetime cannabis users met the DSM's Third Edition, Revised criteria for dependence at some time in their life, compared to 32% of tobacco users, 23% of opiate users, and 15% of alcohol users (Anthony et al., 1997). The National Epidemiologic Survey on Alcohol and Related Conditions also reported that there was a 9% lifetime cumulative probability of transitioning from marijuana use to dependence, with a higher risk of dependence in individuals with a history of psychiatric or substance dependence comorbidity (Lopez-Quintero et al., 2011). In the United States, data from the 2020 NSDUH show that ~14 million individuals (5.1%) aged 12 or older who use marijuana or other cannabinoid preparations met criteria for CUD.

Individuals who develop a substance use disorder, including CUD, may seek treatment for the disorder. From 2015 to 2020, TEDS documented approximately 10.8 million treatment-episode admissions reported by individuals treated at publicly funded substance use treatment programs. Out of 1.4 million treatment admissions documented by TEDS in 2020, marijuana was reported as the primary substance of abuse in approximately 10% of admissions, making it the third most frequently reported primary substance of abuse, after alcohol (31.2%) and heroin (20.6%). A similar pattern was seen from 2015-2019 for these three substances.

During 2015 to 2020, the proportion of admissions where marijuana was reported as the primary substance of abuse declined each year from 14% in 2015 to 10% in 2020. The data for heroin and alcohol show a similar reduction over time. The proportion of admissions where heroin was reported as the primary substance of abuse was ~26% from 2015-2018, decreasing to 23% in 2019 and further decreasing to 21% in 2020. For admissions where alcohol was reported as the primary substance of abuse, the proportion of admissions for this substance decreased each year from 33% in 2015 to 30% in 2018 before increasing slightly to 31% in 2019 and 2020. In contrast, the proportion of admissions where cocaine was reported as the primary substance of abuse stayed stable from 2015 to 2020 at 5-6% each year, while a similar pattern of stable admission data over time was seen for benzodiazepines (~1% from 2015-2020).

In conclusion, the animal behavioral data show that $\Delta 9$ -THC produces rewarding properties that underlie the abuse potential of marijuana. Epidemiological data demonstrate that some

individuals who use marijuana for its rewarding properties go on to develop CUD, which shows that marijuana can produce psychological dependence. Among those individuals who seek treatment for a substance use disorder (psychological dependence) on a drug of abuse, treatment for CUD (psychological dependence on marijuana as the primary substance of abuse) was the third most frequently reported reason for admission for treatment. Thus, marijuana can produce psychic dependence in some individuals who use the drug.

Physical Dependence

Physical dependence is a state of adaptation, manifested by a drug-class specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. Although physical dependence is often associated with addiction, it can be produced by repeated administration of drugs both with and without abuse potential.

As described in Factor 2, Δ^9 -THC (the primary compound responsible for the abuse potential of marijuana) is an agonist at CB₁ receptors. When marijuana (or isolated Δ^9 -THC) is administered chronically, there is a down-regulation of CB₁ receptors, which leads to behavioral tolerance (Gonzalez et al., 2005; Lichtman & Martin, 2005). The underlying mechanism for marijuana withdrawal appears to be the uncoupling and/or desensitization of CB₁ receptors that precedes receptor down-regulation (Breivogel et al., 2003). Abrupt discontinuation of marijuana after prolonged administration produces withdrawal symptoms in rats and in humans that are typically opposite to those that occur with activation of the CB₁ receptor (Budney et al., 2004; Haney et al., 2005). Precipitated withdrawal can also be induced with administration of CB₁ antagonists following chronic administration (Lichtman et al., 2001; Wilson et al., 2006), while administration of CB₁ agonists can attenuate some withdrawal symptoms associated with marijuana discontinuation (Allsop et al., 2014; Haney et al., 2008; Haney et al., 2004; Trigo et al., 2016). These data confirm the importance of the CB₁ receptor in marijuana physical dependence.

The occurrence of withdrawal symptoms in individuals who use marijuana who only use the drug occasionally has not been established (Budney & Hughes, 2006). However, in heavy, chronic individuals who use marijuana, drug discontinuation can lead to a withdrawal syndrome (Budney & Hughes, 2006; Haney et al., 1999). Most marijuana withdrawal symptoms begin within 24-48 hours of drug discontinuation, peak within 2-6 days, and reduce over 1-2 weeks as Δ^9 -THC levels decline (Connor et al., 2021).

The most commonly reported withdrawal symptoms from clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness (Haney et al., 2008; Haney et al., 2004; Haney et al., 1999; Vandrey et al., 2008). Less commonly reported withdrawal symptoms include depressed mood, sweating, shakiness, physical discomfort, and chills (Budney & Hughes, 2006; Haney et al., 1999). The DSM-V lists symptoms of “cannabis withdrawal” that are similar in scope to those reported in the experimental studies and include: nervousness or anxiety, irritability or aggression, insomnia or unpleasant dreams, depressed mood, decreased appetite or weight loss,

restlessness, abdominal pain, shakiness or tremors, sweating, fever, chills, and headache (American Psychiatric Association, 2013).

The drug label for Marinol, which contains Δ 9-THC (as dronabinol), describes a similar withdrawal syndrome following repeated drug use and discontinuation in Section 9.3 Dependence:

"A withdrawal syndrome was reported after the abrupt discontinuation of dronabinol capsules in subjects receiving dosages of 210 mg per day for 12 to 16 consecutive days. Within 12 hours after discontinuation, subjects manifested symptoms such as irritability, insomnia, and restlessness. By approximately 24 hours post-dronabinol discontinuation, withdrawal symptoms intensified to include "hot flashes", sweating, rhinorrhea, loose stools, hiccoughs, and anorexia. These withdrawal symptoms gradually dissipated over the next 48 hours.

Electroencephalographic changes consistent with the effects of drug withdrawal (hyperexcitation) were recorded in patients after abrupt dechallenge. Patients also complained of disturbed sleep for several weeks after discontinuing therapy with high dosages of dronabinol."

Physical dependence may occur in up to 40-50% of individuals who use marijuana on a regular basis (Kesner & Lovinger, 2021). A meta-analysis of 23,518 individuals who frequently used marijuana showed that 47% of subjects reported symptoms of marijuana withdrawal, as evaluated by standardized scales (Bahji et al., 2020). When the data were sorted by various samples, the prevalence of physical dependence was 54% in outpatient samples and 17% in community samples. However, when samples from individuals who were inpatients in drug abuse treatment centers were evaluated, the prevalence of physical dependence was 87%. This is consistent with data showing that 90% of individuals who use marijuana who were diagnosed with CUD also reported marijuana physical dependence (Bonnet & Preuss, 2017). For those individuals with CUD, the severity and duration of withdrawal symptoms associated with marijuana discontinuation are greater than in those who do not have a diagnosis of CUD. This may be a function of individuals with CUD having a more extensive exposure to marijuana (Connor et al., 2021).

The marijuana withdrawal syndrome appears to be relatively mild compared to the withdrawal syndrome associated with alcohol which can include more serious symptoms such as agitation, paranoia, seizures and even death. Multiple studies comparing the withdrawal symptoms associated with marijuana and tobacco (not scheduled in the CSA) demonstrate that the magnitude and time course of the two withdrawal syndromes are similar (Budney et al., 2008; Vandrey et al., 2008; Vandrey et al., 2005). Animal studies have shown that after short-term administration of equianalgesic doses of heroin and Δ 9-THC to monkeys, withdrawal signs were observed after heroin administration but not after Δ 9-THC administration (Ding et al., 2023), further demonstrating the decreased magnitude of withdrawal symptoms associated with marijuana relative to other drug classes.

Conclusions

In conclusion, experimental data and clinical reports demonstrate that chronic, but not acute, use of marijuana can produce both psychic and physical dependence in humans. Epidemiological data provided in greater detail in Factors 4 and 5 provide additional evidence of psychic dependence. The symptoms associated with both kinds of dependence are relatively mild for most individuals, although the severity may be greater with increased exposure to marijuana.

FACTOR 8. WHETHER THE SUBSTANCE IS AN IMMEDIATE PRECURSOR OF A SUBSTANCE ALREADY CONTROLLED UNDER THIS ARTICLE

Under the eighth factor, the Secretary must consider whether marijuana is an immediate precursor of a controlled substance. Marijuana is not an immediate precursor of another controlled substance.

III. RECOMMENDATION

Upon consideration of the eight factors determinative of control of a substance (21 U.S.C. 811(c)), FDA recommends that marijuana be rescheduled from Schedule I to Schedule III of the CSA. NIDA concurs with this scheduling recommendation. Marijuana meets the three criteria for placing a substance in Schedule III of the CSA, as set forth under 21 U.S.C. 812(b)(3):

1. Marijuana has a potential for abuse less than the drugs or other substances in Schedules I and II.

Marijuana contains Δ^9 -THC (also known as dronabinol when specifically referring to (-)-*trans*- Δ^9 -THC stereoisomer), the substance responsible for the abuse potential of marijuana. Δ^9 -THC has agonist properties at CB₁ cannabinoid receptors and produces rewarding responses in animals, as evidenced by its ability to produce self-administration and conditioned place preference. When marijuana is administered to humans under experimental conditions, it produces a wide range of positive subjective responses, in addition to certain negative subjective responses. Common responses to marijuana when it is used by individuals for nonmedical purposes include euphoria and other positive subjective responses, as well as perceptual changes, sedative responses, anxiety responses, psychiatric, social, and cognitive changes, and physiological changes.

Epidemiological data from NSDUH show that marijuana is the most frequently abused federally illicit drug in the United States on a past-year and past-month basis among the illicit comparator drugs considered. Although 50% of respondents in NSDUH reported using marijuana nonmedically less than 5 days per month, another 30% reported using it nonmedically for 20 days or more per month.

Despite the high prevalence of nonmedical use of marijuana, an overall evaluation of epidemiological indicators suggests that it does not produce serious outcomes compared to drugs in Schedules I or II. This is especially notable given the availability to marijuana consumers of marijuana and marijuana-derived products that contain extremely high levels of Δ^9 -THC. Due to such availability, the epidemiological data described in this evaluation inherently include the outcomes from individuals who use marijuana and marijuana-derived products that have doses of Δ^9 -THC that range from low to very high, and yet the data demonstrate that these products overall are producing fewer negative outcomes than drugs in Schedules I or II.

To illustrate this point, when a rank ordering of selected drugs that are abused was compared for various epidemiological measures, it showed that marijuana was among the drugs at the very lowest ranking for: poison control abuse cases, likelihood that any use would lead to a poison control call, accidental/unintentional poisoning, utilization-adjusted rates of unintentional exposure, utilization-adjusted and population-adjusted rates for ED visits and hospitalizations, likelihood of being diagnosed with a serious SUD, deaths reported to poison control centers, and overdose deaths when used with other drugs or as a single substance (as total numbers and when utilization-adjusted). In contrast, comparators such as heroin (Schedule I), oxycodone (Schedule II), and cocaine (Schedule II) typically were in the highest rank ordering on these measures.

For the various epidemiological measures evaluated above, it should be noted that marijuana was also compared to controlled substances in Schedule III (ketamine) and Schedule IV (benzodiazepines, zolpidem, and tramadol), as well as to other Schedule II substances (fentanyl and hydrocodone). The analyses were conducted in this manner to provide a comprehensive assessment of the relative abuse potential of marijuana. However, the rank order of these substances regarding harms does not consistently align with the relative scheduling placement of these drugs in the CSA due to the pharmacological differences between various classes of drugs. There are a number of confounding factors that likely influence the adverse outcomes measured in various epidemiological databases and account for the rank ordering of the drugs evaluated on these measures. For example, each substance has associated with it a different population that abuse that substance, a different prevalence of abuse, and a different profile of severe adverse outcomes in a setting of nonmedical use and abuse. Thus, it is challenging to reconcile the ranking of relative harms associated with the comparators used in this evaluation when the rankings differ across various epidemiological databases, and when these rankings often do not align with the scheduling placement of these comparators under the CSA. To address these challenges, we evaluated the totality of the available data and have concluded that it supports the placement of marijuana in Schedule III. Overall, these data demonstrate that, while marijuana is associated with a high prevalence of abuse, the profile of and propensity for serious outcomes related to that abuse lead to a conclusion that marijuana is most appropriately controlled in Schedule III under the CSA.

2. Marijuana has a currently accepted medical use in treatment in the United States.

HHS utilized a two-part test (referred to in this document as the “CAMU test”) that took into account the current widespread medical use of marijuana under the supervision of licensed HCPs under state-authorized programs to evaluate whether the substance has CAMU in the United States. Under Part 1 of the CAMU test, OASH concluded there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented state-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these state jurisdictions. OASH concluded the findings from Part 1 warranted an FDA assessment under Part 2 of the CAMU test to determine if there exists credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied. Part 2 of the CAMU test was conducted based on systematic reviews of studies investigating the safety and efficacy/effectiveness of marijuana, review of relevant professional societies’ position statements, data from state medical marijuana programs and United States national surveys, and review of the labeling of FDA-approved products relevant to the analysis.

Based on the totality of the available data, there exists some credible scientific support for the medical use of marijuana in at least one of the indications for which there is widespread current experience by HCPs in the United States, as identified by OASH under Part 1 of the CAMU test. Seven indications were selected by FDA for consideration under Part 2 of the CAMU test. These indications included anorexia related to a medical condition, anxiety, epilepsy, inflammatory bowel disease, nausea and vomiting (e.g., chemotherapy-induced), pain, and post-traumatic stress disorder. The analysis of, and conclusions regarding, the available data are not meant to imply that safety and effectiveness have been established for marijuana that would

support FDA approval of marijuana for a particular indication. However, the available data do provide some credible level of scientific support for some of the therapeutic uses for which marijuana is being used in clinical practice in the United States. Thus, based on the widespread HCP experience and the extent of medical use evaluated by OASH under the Part 1 test, and the determination of some credible scientific support for at least some therapeutic uses identified in the Part 1 test, for purposes of the drug scheduling criteria in 21 U.S.C. 812(b), marijuana has a currently accepted medical use in the United States, specifically for the treatment of anorexia related to a medical condition, nausea and vomiting (e.g., chemotherapy-induced), and pain.

Additionally, and considering that marijuana is currently controlled in Schedule I of the CSA, we note that one of the criteria for control in Schedule I as set forth in 21 U.S.C. 812(b)(1) is that “(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.” Based on our evaluation of CAMU, as summarized above, we conclude that there is accepted safety for the use of marijuana under medical supervision for the treatment of anorexia related to a medical condition, nausea and vomiting (e.g., chemotherapy-induced), and pain. Thus, even apart from the findings made herein for the current recommendation for Schedule III, this criterion for control in Schedule I as set forth under 21 U.S.C. 812(b)(1)(C) is not met for marijuana.

3. Abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence.

Clinical studies have demonstrated that marijuana produces physical and psychological dependence. Regarding physical dependence, as evidenced by its associated withdrawal symptomology upon abrupt discontinuation of use, the most commonly reported marijuana withdrawal symptoms in clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness. Marijuana withdrawal symptoms typically peak within 2-6 days and decline over 1-2 weeks as Δ 9-THC is eliminated. Similarly, the drug labels for the FDA-approved drug products Marinol and Syndros (both of which contain dronabinol, the (-)-*trans*- Δ 9-THC stereoisomer) state that following chronic administration of dronabinol, drug discontinuation leads to irritability, insomnia, and restlessness at 12 hours and by 24 hours the withdrawal symptoms can include “hot flashes,” sweating, rhinorrhea, diarrhea, and anorexia.

Notably, marijuana withdrawal syndrome has been reported in individuals with heavy, chronic marijuana use, but its occurrence in occasional individuals who use marijuana has not been established. The marijuana withdrawal syndrome appears to be relatively mild compared to the withdrawal syndrome associated with alcohol, which can include more serious symptoms such as agitation, paranoia, seizures and even death. Multiple studies comparing the withdrawal symptoms associated with marijuana and tobacco demonstrate that the magnitude and time course of the two withdrawal syndromes are similar.

The ability of marijuana to produce psychic dependence is shown through its ability to produce rewarding effects that underlie its nonmedical use and epidemiological outcomes related to abuse, as detailed in the first Finding on abuse potential (above).

Thus, abuse of marijuana may lead to moderate or low physical dependence, depending on frequency and degree of marijuana exposure. It can produce psychic dependence in some individuals, but the likelihood of serious outcomes is low, suggesting that high psychological dependence does not occur in most individuals who use marijuana.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Office of the Assistant Secretary for Health
Washington, D.C. 20201

DATE: July 17, 2023

TO: Commissioner, Food and Drug Administration (FDA)

FROM: The Assistant Secretary for Health,
Office of the Assistant Secretary of Health (OASH)

SUBJECT: Part 1 Analysis

EXECUTIVE SUMMARY

The Department of Health and Human Services (HHS) has updated its analysis of a substance's "currently accepted medical use in treatment in the United States" ("CAMU") for purposes of the Controlled Substances Act (CSA), 21 U.S.C. § 812(b)(1). As part of this analysis, HHS includes consideration of whether there is (1) widespread current experience with medical use of the substance in the United States by licensed health care practitioners (HCPs) operating in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine ("Part 1"), and (2) whether there is scientific support for at least one of these medical uses of a substance ("Part 2"). To assist in the determination of whether marijuana has a CAMU in the United States, OASH conducted an analysis evaluating Part 1 and confirmed that more than 30,000 HCPs across 43 U.S. jurisdictions are authorized to recommend the medical use of marijuana for more than six million registered patients for at least 15 medical conditions. OASH's Part 1 analysis, therefore, supports the finding that marijuana has at least one CAMU in the United States. Additional analysis is required for evaluating Part 2 of the CAMU analysis, which considers whether there exists some credible scientific support for the use of marijuana for at least one of the medical conditions.

REQUEST

On October 6, 2022, President Biden directed the Secretary of HHS and the Attorney General to review how marijuana is currently scheduled under federal law.¹ The purpose of this memorandum is to share the findings from Part 1 and request that your Agency conduct Part 2 of the analysis to assess if there exists credible scientific support for the use of marijuana for at least one medical condition identified in this memorandum.

¹ <https://www.whitehouse.gov/briefing-room/statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform/>

BACKGROUND

Under the CSA, marijuana is currently a Schedule I substance in the United States.² Schedule I is a category for substances that are considered to have a high potential for abuse, have no CAMU in the United States, and lack accepted safety for use under medical supervision.

HHS's CAMU analysis has two parts.

- **Part 1:** There exists widespread, current experience with medical use of the substance by HCPs operating in accordance with implemented jurisdiction-authorized programs, where medical use is recognized by entities that regulate the practice of medicine. Part 1 of this approach is supported by factors such as the following (with none being dispositive):
 - a) Whether a substantial number of HCPs have gained clinical experience with at least one specific medical use of the substance under existing and implemented state authorized programs;
 - b) Whether a substantial number of entities that regulate the practice of medicine recognize at least one specific medical use of the substance; and
 - c) Whether an HCPs' clinical experience with the medical use of the substance is of sufficient extent and duration to help evaluate potential clinical uses and longer-term toxicities and potential harms of the substance when used under medical supervision.
- **Part 2:** There exists some credible scientific support for at least one of the medical uses for which Part 1 is met.

METHODOLOGY AND TERMINOLOGY

To evaluate if marijuana meets one or more of the three Part 1 factors, OASH applied the Part 1 approach described above to currently available data on the medical use(s) of marijuana in the United States. With input from other federal agencies, OASH collected pertinent programmatic and policy data, including data from states' websites, and other publicly available sources (secondary data condensed for this memo). The findings below and in TAB A are based on an interpretation of that information.

For the purposes of this memo, states and territories are henceforth referred to as 'jurisdictions.' 'Regulatory entities,' which vary widely by state, refers to the jurisdictions' respective entities which oversee implementation of the relevant marijuana for medical use statute. Additionally, 'reviewing/recommending bodies' refers to an entity that conducts a jurisdiction-level scientific medical review for the purpose of evaluating marijuana for medical use(s) and make a recommendation to the regulatory entity. Further, marijuana for medical use(s) may be directed by a ballot initiative or other legal authorization, which was not evaluated for purposes of this memo.

² 21 U.S.C. § 812(c)(1)(B)

FINDINGS:

A summary of the Part 1 key findings and conclusions used to assess widespread, current experience with medical use of marijuana and whether it has a CAMU is listed below. Data for individual jurisdictions are provided in the tables and figures in TAB A. Part 1 uses data and information collected up to March 29, 2023.

Factor 1(a) – Whether a substantial number of licensed health care practitioners have gained clinical experience with at least one specific medical use of the substance under existing and implemented state-authorized programs.

Factor 1(a) Findings: There exists significant variability in HCPs' clinical experience with recommending marijuana for medical use. Some reasons for the variability include: 1) the number of HCPs authorized by a jurisdiction to recommend marijuana for medical conditions, 2) the length of time a jurisdiction has had a marijuana for medical use program in place, 3) the educational requirements needed for HCPs to be authorized to recommend marijuana for medical conditions; 4) the number of patients who are registered in a jurisdiction to participate in marijuana for medical use programs; and 5) the availability of individual level practitioner data surrounding recommendation patterns for qualifying medical conditions.

- Currently, more than 30,000 HCPs are authorized to recommend the use of marijuana for more than six million patients with medical conditions that are enrolled in authorized marijuana for medical use programs (Table 4).
- Ten jurisdictions require specific HCP education on the use of marijuana prior to recommending marijuana for medical conditions, and two of these states require HCPs to pass an exam for certification (Table 2b).
- Because HCP-level data on the provision of marijuana prescriptions for specific medical conditions is unavailable, data on patient-reported medical conditions authorized by HCPs was used as a surrogate measure for providers' clinical experience (Figure 1).
- The number of patients enrolled in marijuana for medical use programs who use it for chronic pain, post-traumatic stress disorder (PTSD), arthritis, and cancer increased from 2016 through 2020 (Figure 1).

Factor 1(a) Conclusion: Taken together, the data support that a substantial number of HCPs have gained clinical experience with at least one specific medical use of marijuana under state-authorized programs.

Factor 1(b) – Whether a substantial number of entities that regulate the practice of medicine recognize at least one specific medical use of the substance.

Factor 1(b) Findings: The identified secondary data show that, across jurisdictions that conduct medical or scientific reviews prior to authorizing marijuana for particular medical use(s), 'reviewing/recommending bodies' are not necessarily the same entities that regulate the practice of medicine more generally. However, marijuana for medical use programs within these jurisdictions have included provisions for a board of qualified experts to evaluate the inclusion of additional qualifying medical conditions to those specified in a jurisdiction's law. These boards make their determinations through a process of reviewing available research as well as

considering expert and public testimony. As noted, regulatory entities with oversight of the medical use of marijuana under each jurisdiction varies widely. For example, a state Department of Health, Department of Revenue, Department of Finance, Public Safety, Board of Pharmacy, and Alcohol Control Office may have varying degrees of oversight in their jurisdiction. A review of secondary data analyzed shows that the specific type and number of qualifying medical conditions recognized by jurisdictions varies, as does the medical or scientific evidence referenced to support adding to each jurisdiction's list of qualifying medical conditions.

Thirty-eight states, the District of Columbia, and four territories³ have laws that authorize the use of marijuana for medical use(s) (Table 1). These efforts reflect actions taken to implement programs to assess and oversee the use of marijuana in their jurisdiction.

- Seventeen jurisdictions have added conditions through a medical review process (Table 2a).
- Twenty-one of the marijuana for medical use programs include provisions for a board of qualified experts to determine the inclusion of additional qualifying medical conditions to those specified in the law.⁴
- The Prescription Drug Monitoring Training and Technical Assistance Center (PDMP TTAC) tracks PDMP data, under a grant funded from the Bureau of Justice Assistance. TTAC information is reported from two sources: PDMP Administrators and a review of laws and regulations. TTAC sends out an annual survey (>90% response rate) to the respective PDMP Administrators to determine their current policies and capabilities. All 50 states, the District of Columbia, Guam, Puerto Rico, and the Northern Mariana Islands received this survey; it was not sent to the U.S. Virgin Islands as they do not have a PDMP tracking program. TTAC reports marijuana for medical use information. Such information was reported or available through the PDMP in the following jurisdictions: Arizona, Connecticut, Illinois, Massachusetts, New Jersey, New York, North Dakota, Ohio, Oklahoma, Pennsylvania, Utah, Vermont, Virginia.⁵
- Additionally, TTAC also reports specific requirements around PDMP HCP checks.⁶ Examples requiring provider checks were identified by TTAC as follows:
 1. Florida - provides that a qualified physician may issue a physician certification for the medical use of marijuana only if the physician has reviewed the patient's-controlled drug prescription history in the PDMP.
 2. Louisiana - an emergency rule, effective 8/1/2020, includes a requirement that prior to dispensing any marijuana product to a patient, the marijuana product dispensing pharmacist shall review the patient's records in the Louisiana prescription monitoring program.

³ <https://www.ncsl.org/health/state-medical-cannabis-laws>, see Table 1.

⁴ https://assets.nationbuilder.com/americansforsafeaccess/pages/27187/attachments/original/1675362731/StateoftheStates22_P5.pdf?1675362731

⁵ <https://www.pdmpassist.org/Policies/Maps/PDMPpolicies>

⁶ https://www.pdmpassist.org/pdf/Mandatory_Query_Conditions.pdf

3. Massachusetts - before issuing a written certification for marijuana, a certifying healthcare provider must query the PDMP and review the qualifying patient's prescription history, unless otherwise specified by the Commission.
 4. New York - requires practitioners to consult the PDMP prior to making or issuing a certification of a serious condition requiring the use of marijuana; requires dispensers to check the PDMP to ensure that a patient is not receiving greater than a 30-day supply.
 5. Rhode Island - requires practitioners query the PDMP prior to issuing a written certification for marijuana and make a judgment about the potential for drug-drug interactions, adverse events, or untoward clinical outcomes from adding marijuana.
 6. Utah - any qualified medical provider, who recommends or renews a recommendation for marijuana, to review any record related to the patient in the state's electronic verification system and the controlled substances database.
- A substantial number of jurisdictions have written procedures for addressing complaints, adverse events, and recalls in marijuana dispensaries (Table 2b).⁴
 - A substantial number of jurisdictions recognize the use of marijuana for various medical conditions such as Amyotrophic Lateral Sclerosis (ALS) (36), Autism Spectrum Disorder (34), cachexia (29), cancer (40), conditions causing chronic or intractable pain (40), Crohn's Disease (34), epilepsy or other conditions causing seizures (39), glaucoma (36), HIV/AIDS (39), Multiple Sclerosis (39), Parkinson's Disease (35), persistent/severe muscle spasm (33), persistent/severe nausea (33), PTSD (39), spasticity (31) (Table 3).

Factor 1(b) Conclusion: The above summary and attached tables demonstrate that a substantial number of regulatory entities recognize at least one specific medical use of the substance.

Factor 1(c) – Whether licensed health care practitioners' clinical experience with the medical use of the substance is of sufficient extent and duration to help evaluate potential clinical uses and longer-term toxicities and potential harms of the substance when used under medical supervision.

Factor 1(c) Findings:

- Approximately six million individual U.S. patients are currently registered in programs that authorize the use of marijuana for various medical conditions, with 14 jurisdictions having more than 100,000 registered patients (Table 4).
- Between 1996-2000, eight jurisdictions legalized marijuana for medical use in the United States (Table 1 and Figure 1), and currently several jurisdictions have documented processes to track adverse events, complaints, and recalls (Table 2b).
- A substantial number of jurisdictions require the HCP to have an established, bona-fide, relationship with the patient. Some require a specific duration of follow up with patients after recommending marijuana for medical use.

Factor 1(c) Conclusion: The above summary and attached tables and figure demonstrate that HCPs' clinical experience with the use of marijuana for various medical conditions is of sufficient extent and duration to help evaluate potential clinical uses. However, based on the available secondary data for this analysis, it could not be conclusively determined whether HCP clinical experience with the use of marijuana is of sufficient extent and duration to help evaluate

the longer-term toxicities and potential harms of marijuana when used under medical supervision.

SUMMARY OF CONCLUSIONS

OASH's Part 1 analysis confirmed that more than 30,000 HCPs are certified to recommend the use of marijuana for more than six million registered patients, constituting widespread clinical experience associated with various medical conditions recognized by a substantial number of jurisdictions across the United States. For several jurisdictions, these programs have been in place for several years, and include features that actively monitor medical use and product quality characteristics of marijuana dispensed. Taken together, the findings from Part 1 warrant an FDA assessment under Part 2 of the Department's CAMU approach to determine if there exists credible scientific support for the use of marijuana for at least one of the medical conditions listed in Table 3.

A handwritten signature in black ink, appearing to read 'Q22 MP'.

Rachel L. Levine, M.D.
ADM, USPHS

Attachments

TAB A: Tables 1, 2a, 2b, 3 and 4; Figure 1

Table 1: Year of Legalization and Implementation of the Medical Use of Marijuana in the U.S.

U.S Jurisdiction	Year Legalized ^a	Year Implemented ^b
Alabama	2021	2023
Alaska	1999	2016
Arizona	2010	2012
Arkansas	2016	2019
California	1996	2018
Colorado	2000	2014
Connecticut	2012	2017
Delaware	2011	2015
District of Columbia	2011	2013
Florida	2016	2016
Guam	2014	NA
Hawaii	2000	2017
Illinois	2013	2015
Iowa	2017	2018
Louisiana	2015	2019
Maine	1999	2011
Maryland	2013	2017
Massachusetts	2012	2015
Michigan	2008	2018
Minnesota	2014	2015
Mississippi	2022	2023
Missouri	2018	2020
Montana	2004	2018
Nevada	1998	2015
New Hampshire	2013	2016
New Jersey	2010	2012
New Mexico	2007	2010
New York	2014	2016
North Dakota	2016	2019
The Northern Mariana Islands	2018	2021
Ohio	2016	2019
Oklahoma	2018	2018
Oregon	1998	2015
Pennsylvania	2016	2018
Puerto Rico	2016	2017
Rhode Island	2006	2013

U.S Jurisdiction	Year Legalized ^a	Year Implemented ^b
Table 1, continued		
South Dakota	2020	2022
Utah	2018	2020
Vermont	2004	2013
Virginia	2020	2020
Washington	1998	2016
West Virginia	2017	2021
US Virgin Islands	2019	2023
^a Year legalized refers to the year statute was enacted. ^b Year implemented refers to the year in which the first dispensary opened.		

Table 2a: U.S. Jurisdictions That Conduct Medical or Scientific Review Prior to Recognizing a Medical Condition as Appropriate for Marijuana Use.

U.S Jurisdiction	Approved After Medical or Scientific Review (Yes/No)	Reviewing/ Recommending Bodies	Medical Conditions Recognized	Medical Conditions Denied (Listed or 'No')
Connecticut	Yes	Department of Consumer Protection/Board of Physicians	<ul style="list-style-type: none"> • Post Laminectomy Syndrome with Chronic Radiculopathy • Severe Psoriasis • Psoriatic Arthritis • Amyotrophic Lateral Sclerosis (ALS) • Ulcerative Colitis • Complex Regional Pain Syndrome Type 1 and Type II • Sickle Cell Disease • Spasticity • Neuropathic Pain Associated with Osteogenesis Imperfecta • Chronic Neuropathic Pain Associated with Degenerative Spinal Disorders • Interstitial Cystitis • MALS Syndrome (Median Arcuate Ligament Syndrome) • Vulvodynia • Vulvar Burning • Intractable Neuropathic Pain, unresponsive to standard medical treatments • Tourette Syndrome • Chronic Pain of at least 6 months duration, associated with a specified underlying chronic condition refractory to other treatment intervention • Ehlers-Danlos Syndrome Associated with Chronic Pain • Chronic Pancreatitis • Movement disorders associated with Huntington 	No

U.S Jurisdiction	Approved After Medical or Scientific Review (Yes/No)	Reviewing/ Recommending Bodies	Medical Conditions Recognized	Medical Conditions Denied (Listed or 'No')
Table 2a, continued				
Delaware	Yes	Delaware Department of Health and Social Services	<ul style="list-style-type: none"> • Autism – pediatric • Autism with Aggressive and/or Self-injurious Behaviors 	<ul style="list-style-type: none"> • Anxiety • Opioid Use Disorder
Florida	Yes	Department of Health	<ul style="list-style-type: none"> • Epilepsy 	No
Guam	Yes	An advisory board of nine (9) members including practitioner a variety of specialty fields	<ul style="list-style-type: none"> • Depression • Anxiety • Sleep disorders • Chronic pain • Autism <p>(added to the list of approved debilitating conditions)</p>	No
Hawaii	Yes	Department of Health	<ul style="list-style-type: none"> • Amyotrophic Lateral Sclerosis (ALS) 	No
Illinois	Yes	Illinois Department of Public Health	<ul style="list-style-type: none"> • Terminal Illness • Autism • Anorexia nervosa • Chronic pain • Ehlers-Danlos syndrome • Irritable bowel syndrome • Migraines • Neuro-Bechet's autoimmune disease • Neuropathy • Osteoarthritis • Polycystic kidney disease (PKD) 	No
Iowa	Yes	Medical Cannabidiol Board and Iowa Board of Medicine	<ul style="list-style-type: none"> • Severe Intractable Pediatric Autism with Self-Injurious Behavior • Corticobasal Degeneration • Intellectual Disability (ID) with Aggression and/or Self-Injury • Ulcerative Colitis 	No

U.S Jurisdiction	Approved After Medical or Scientific Review (Yes/No)	Reviewing/ Recommending Bodies	Medical Conditions Recognized	Medical Conditions Denied (Listed or 'No')
Table 2a, continued				
Michigan	Yes	Licensing and Regulatory Authority Medical Marijuana Review Panel	<ul style="list-style-type: none"> • Cerebral palsy • PTSD (post-traumatic stress disorder) • Autism • Arthritis • Chronic Pain • Colitis • IBS • Obsessive Compulsive Disorder • Parkinson's Disease • Rheumatoid Arthritis • Tourette Syndrome • Ulcerative Colitis 	<ul style="list-style-type: none"> • Chronic Aggressive Behavior
Minnesota	Yes	Department of Health (approved by the Health Commissioner)	<ul style="list-style-type: none"> • Intractable Pain • PTSD (post-traumatic stress disorder) • Autism spectrum disorder • Obstructive sleep apnea • Alzheimer's disease • Chronic pain • Sickle cell disease • Motor or vocal tic disorder • Irritable bowel syndrome • Obsessive compulsive disorder 	No
New Hampshire	Yes	Therapeutic Cannabis Medical Oversight Board	<ul style="list-style-type: none"> • Insomnia • Autism Spectrum Disorder 	<ul style="list-style-type: none"> • Anxiety • Tick-borne illnesses • Opioid use disorder
New Jersey	Yes	State Health Commissioner after review by the Medical Marijuana Review Panel	<ul style="list-style-type: none"> • Tourette Syndrome • Chronic Pain of Visceral Origin • Anxiety • Migraine • Chronic pain related to musculoskeletal disorder • Chronic pancreatitis • Irritable bowel syndrome • Opioid use disorder 	<ul style="list-style-type: none"> • Chronic fatigue syndrome • Asthma

U.S Jurisdiction	Approved After Medical or Scientific Review (Yes/No)	Reviewing/ Recommending Bodies	Medical Conditions Recognized	Medical Conditions Denied (Listed or 'No')
Table 2a, continued				
New Mexico	Yes	Medical Cannabis Medical Advisory Board recommendation / Secretary for the Department of Health	<ul style="list-style-type: none"> • Anxiety Disorder • Depression • ADHD • Autism Spectrum • Dystonia • Migraines • Degenerative Neurological Disorder • Neuroprotective as Approved Conditions • Alzheimer's Disease • Tourette's (Tourette Syndrome) 	<ul style="list-style-type: none"> • Nystagmus • Substance Use Disorder
New York	Yes	State Department of Health (approved by the Commissioner of Health)	<ul style="list-style-type: none"> • Severe debilitating pain • PTSD (post-traumatic stress disorder) • Any condition for which an opioid could be prescribed 	No
Ohio	Yes	State Medical Board of Ohio	<ul style="list-style-type: none"> • Cachexia or wasting syndrome • Huntington's disease • Terminal illness • Spasticity 	<ul style="list-style-type: none"> • Autism • Irritable Bowel Syndrome
Oregon	Yes	Public Health Division, Oregon Health Authority	<ul style="list-style-type: none"> • Cancer • Glaucoma • A degenerative or pervasive neurological condition • HIV/AIDS, a side effect related to the treatment of those medical conditions • Medical conditions or treatment for a medical conditions that produces cachexia • Severe pain • Severe nausea • Seizures • Persistent muscle spasms • PTSD (post-traumatic stress disorder) 	No

U.S Jurisdiction	Approved After Medical or Scientific Review (Yes/No)	Reviewing/ Recommending Bodies	Medical Conditions Recognized	Medical Conditions Denied (Listed or 'No')
Table 2a, continued				
Pennsylvania	Yes	Medical Advisory Board, PA Department of Health	<ul style="list-style-type: none"> • Cancer including remission therapy • Neurodegenerative diseases • Terminal illness • Dyskinetic Spastic movement disorders • Severe Chronic Intractable pain of neuropathic origin • Severe Intractable pain • Opioid use disorder • Anxiety Disorder • Chronic Hepatitis C • Tourette Syndrome 	No
Rhode Island	Yes	Department of Health	<ul style="list-style-type: none"> • Autism Spectrum Disorder • Pain • Nausea and other symptoms associated with certain debilitating medical conditions, as found by the National Academy of Sciences' Institute of Medicine in March 1999 	No

Table 2b: Other Quality Indicators of U.S. Jurisdictions' Programs for Medical Use of Marijuana.

U.S. Jurisdiction	Educational Requirements for Certification	ASA ^a Grade for Dispensary Operations	Patient Level Tracking of Marijuana Dispensed ^b
Alabama	Yes	Yes	No
Alaska	No	No	No
Arizona	No	No	No
Arkansas	No	Yes	No
California	No	Yes	No
Colorado	No	Yes	No
Connecticut	No	Yes	Yes
Delaware	No	No	Yes
District of Columbia	No	No	No
Florida	Yes	Yes	Yes
Guam	No	No	No
Hawaii	No	Yes	No
Illinois	No	Yes	No
Iowa	No	Yes	Yes
Louisiana	No	No	No
Maine	No	No	No
Maryland	No	Yes	No
Massachusetts	Yes	No	Yes
Michigan	No	Yes	No
Minnesota	No	No	No
Mississippi	Yes	No	No
Missouri	No	No	No
Montana	No	Yes	No
Nevada	No	No	No
New Hampshire	No	Yes	No
New Jersey	No	Yes	No
New Mexico	No	Yes	No
New York	Yes	Yes	Yes
North Dakota	No	Yes	No
The Northern Mariana Islands	No	No	No
Ohio	No	No	Yes
Oklahoma	No	No	No
Oregon	No	Yes	No
Pennsylvania	Yes	No	No

U.S. Jurisdiction	Educational Requirements for Certification	ASA ^a Grade for Dispensary Operations	Patient Level Tracking of Marijuana Dispensed ^b
Table 2b, continued			
Puerto Rico	Yes	Yes	No
Rhode Island	No	Yes	Yes
South Dakota	No	No	No
Utah	Yes	No	Yes
Vermont	No	Yes	No
Virginia	No	Yes	No
Washington	Yes	Yes	No
West Virginia	Yes	No	No
US Virgin Islands	No	No	No
^a Americans for Safe Access (ASA) Annual "State of State" report include score cards for each state with a medical cannabis program in place. "Dispensary Operations" are scored on a number of variables. This analysis focuses on one variable of "Dispensary Operations": "adverse event reporting and recall protocol". This provides an impression of whether dispensaries are reporting adverse events and, if so, how they are addressing these reports. Americans for Safe Access Foundation is a non-profit 501(c)(3) organization whose mission is to ensure safe and legal access to cannabis (marijuana) for therapeutic use and research.			
^b Patient Level Tracking: most jurisdictions have "Seed to Sale" tracking; however, based on data provided by the Cannabis Regulators Association (CANNRA) only nine jurisdictions track amounts dispensed to patients.			

Table 3: Medical Conditions Recognized for Medical Use of Marijuana by U.S. Jurisdictions

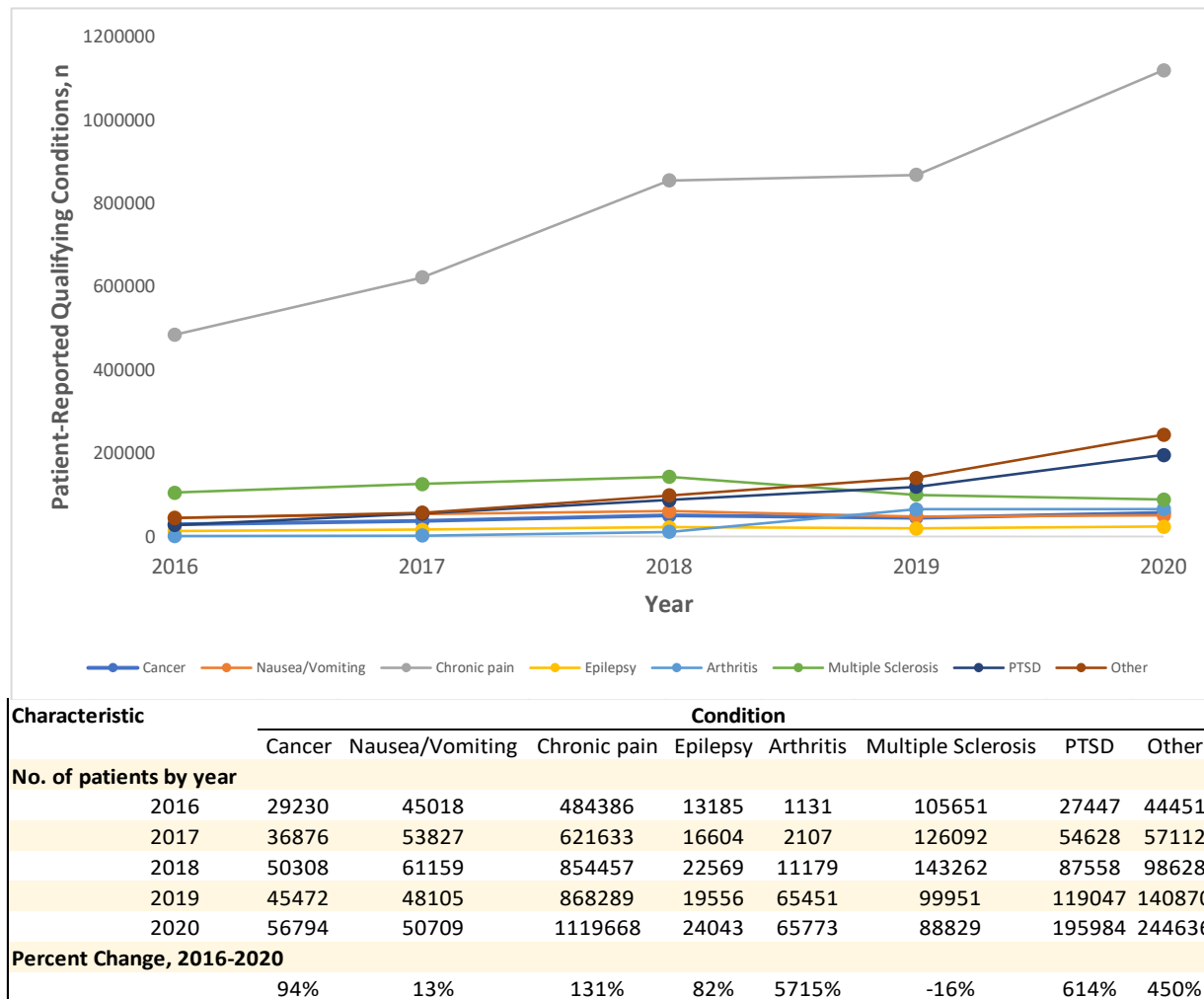
Medical Condition	U.S Jurisdictions	Total Number of Jurisdictions That Recognize the Medical Condition
Amyotrophic Lateral Sclerosis (ALS)	AK, AL, AZ, CA, CT, DC, FL, GU, HI, IA, IL, LA, MA, ME, MI, MD, MN, MO, MS, ND, NJ, NM, NV, NY, NY, OH, OK, PA, OR, RI, SD, USVI, UT, VA, WV, WA	36
Autism Spectrum Disorder	AK, AL, AZ, CA, CO, CT, DE, DC, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, ND, NJ, NM, NV, NY, OK, OR, PA, RI, SD, USVI, UT, VA, WA	34
Cachexia	AK, AL, AZ, CA, CO, CT, DC, DE, GU, HI, IA, IL, LA, MA, MD, MI, MO, MT, ND, NJ, NV, NY, OK, OR, RI, SD, USVI, UT, WA	29
Cancer	AZ, AK, AL, CA, CO, CT, DC, DE, FL, GU, HI, IL, IA, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, UT, VA, VT, WA, WV	40
Condition causing chronic or intractable pain	AK, AL, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, UT, VA, VT, WA, WV	40
Crohn's Disease	AK, AL, AZ, CA, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MO, MS, MT, ND, NJ, NV, OH, OK, OR, PA, RI, SD, UT, VA, VT, WA, WV	34
Epilepsy or condition causing seizures	AK, AL, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, UT, VA, VT, WA, WV	39
Glaucoma	AK, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, VA, VT, WA	36
HIV/AIDs positive	AK, AL, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, UT, VT, WA, WV	39

Medical Condition	U.S Jurisdictions	Total Number of Jurisdictions That Recognize the Medical Condition
Table 3, continued		
Multiple Sclerosis	AK, AL, AZ, CA, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, UT, VA, VT, WA, WV	39
Parkinson's Disease	AK, AL, AZ, CA, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MO, MS, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, SD, USVI, VA, VT, WA, WV	35
Persistent/severe muscle spasm	AK, AL, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IL, LA, MA, MD, ME, MI, MN, MO, MT, ND, NJ, NM, NV, NY, OK, OR, PR, RI, SD, USVI, UT, WA	33
Persistent/severe nausea	AK, AL, AZ, CA, CO, DC, DE, FL, GU, HI, IA, IL, MA, MD, ME, MI, MO, MS, MT, ND, NJ, NM, NV, NY, PR, OK, OR, RI, SD, USVI, UT, VT, WA	33
Post-Traumatic Stress Disorder (PTSD)	AK, AL, AZ, CA, CO, CT, DC, DE, FL, GU, HI, IA, IL, LA, MA, MD, ME, MI, MN, MO, MS, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, PR, RI, USVI, UT, VA, VT, WA, WV	39
Spasticity	AK, AL, AZ, CA, CT, DC, DE, FL, GU, HI, IL, LA, MA, MD, ME, MI, MO, MT, ND, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SD, WA, WV	31
Note: This list includes all mechanisms for recognizing qualifying conditions to include ballot initiatives, legislation, and clinical/scientific review. Numbers include states/territories in which the specific condition is not named, but alternative situations allow for treatment for corresponding condition in that category.		

Table 4: Number of Certified Practitioners and Registered Patients Across U.S. Jurisdictions Medical Use Programs

U.S. Jurisdiction	Number of Certified Practitioners	Timeframe for Practitioner Data	Number of Registered Patients ^a
Alabama	MISSING ^b	MISSING	0
Alaska	MISSING	MISSING	404
Arizona	1,667	March 23, 2023	129,836
Arkansas	989	July 1, 202- June 30, 2022	90,266
California	MISSING	MISSING	MISSING
Colorado	306	January 1, 2022 -December 21, 2022	71,536
Connecticut	1,667	March 31, 2023	49,780
Delaware	467	2021	19,715
District of Columbia	602	December 2021	16,348
Florida	2,563	October 1, 2020 -September 30, 2021	778,781
Guam	0	2019	0
Hawaii	35	May 2021	33,424
Illinois	5,300	Between July 1, 2019 - June 30, 2020	136,574
Iowa	1,821	July 2022	11,676
Louisiana	219	Second Quarter 2021	20,321
Maine	753	2021	106,164
Maryland	1,135	April 5, 2023	161,722
Massachusetts	358	September, 2022	97,003
Michigan	243	February 28, 2023	184,564
Minnesota	2,303	February 2, 2023	39,552
Mississippi	122	December, 2022	0
Missouri	MISSING	January 1, 2022 - Dec. 21, 2022	204,165
Montana	267	January 1, 2020	40,801
Nevada	979	January, 2023	12,788
New Hampshire	1,273	July 2020-June 2021	12,237
New Jersey	1,012	April 13, 2023	112,404
New Mexico	MISSING	MISSING	112,426
New York	4,033	April 1, 2023	123,391
North Dakota	340	June 30, 2022	8,898
The Northern Mariana Islands	MISSING	MISSING	0
Ohio	660	March 8, 2023	317,018
Oklahoma	MISSING	MISSING	374,077
Oregon	1,333	January, 2023	17,957
Pennsylvania	1,812	January, 2023	423,443
Puerto Rico	MISSING	MISSING	118,007

U.S. Jurisdiction	Number of Certified Practitioners	Timeframe for Practitioner Data	Number of Registered Patients ^a
Table 4, continued			
Rhode Island	MISSING	MISSING	16,462
South Dakota	208	April 3, 2023	6,166
Utah	673	April, 2023	61,991
Vermont	MISSING	MISSING	4,302
Virginia	938	January, 2023	52,810
Washington	MISSING	MISSING	52,479
West Virginia	131	March 31, 2023	7,000
US Virgin Islands	MISSING	MISSING	0
^a Americans for Safe Access (ASA) Foundation is a non-profit 501(c)(3) organization whose mission is to ensure safe and legal access to cannabis (marijuana) for therapeutic use and research https://www.asafoundation.org/ .			
^b Missing: data marked "missing" indicative of a) states not tracking data, b) states tracking data but the data is not available or c) it is unknown whether the state tracks the data.			

Figure 1. Substantial Increase in Marijuana Use for Chronic Pain, PTSD, Arthritis & Cancer, 2016-2020^a

Note. Adapted from “U.S. Trends in Registration for Medical Cannabis and Reasons for Use From 2016 to 2020” by Boehnke, KF, Dean, O, Haffajee, RL, and Hosanagar, A., 2022, *Annals of Internal Medicine*, 175(7), p. 948. Includes patient-reported qualifying conditions in medical-only marijuana use states: Arkansas, Arizona, Delaware, Hawai’i, Maryland, Minnesota, Missouri, Montana, New Hampshire, New Mexico, North Dakota, Ohio, Rhode Island, Utah

Considerations for Whether Marijuana Has a Currently Accepted Medical Use in the United States for Purposes of Section 202(b) of the Controlled Substances Act

**Report prepared by the Food and Drug Administration's Center for Drug
Evaluation and Research (CDER), by personnel located in CDER's:**

Office of the Center Director's Controlled Substance Staff

and

**Office of Surveillance and Epidemiology's Office of Pharmacovigilance and
Epidemiology, Division of Epidemiology I**

August 28, 2023

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Glossary

AAFP	American Academy of Family Physicians
AAN	American Academy of Neurology
AAPOR	American Association for Public Opinion Research
AASM	American Academy of Sleep Medicine
AE	adverse event
AHRQ	Agency for Healthcare Research and Quality
AIDS	acquired immunodeficiency syndrome
APA	American Psychiatric Association
ASAM	American Society of Addiction Medicine
BRFSS	Behavioral Risk Factor Surveillance System
CAERS	CFSAN Adverse Event Reporting System
CAMU	currently accepted medical use in treatment in the United States
CAPS-5	Clinician-Administered PTSD Scale for Diagnostic and Statistical Manual of Mental Disorders
CBD	cannabidiol
CDAI	Crohn's disease activity index
CFSAN	Center for Food Safety and Applied Nutrition
CI	confidence interval
CPPC	Cannabis Public Policy Consulting
CSA	Controlled Substances Act
Δ 9-THC	delta-9-tetrahydrocannabinol
DAWN	Drug Abuse Warning Network
DEA	Drug Enforcement Administration
DEPI	Division of Epidemiology I
DSM	Diagnostic and Statistical Manual of Mental Disorders
FAERS	FDA Adverse Event Reporting System
FDA	Food and Drug Administration
FR	<i>Federal Register</i>
GRADE	grading of recommendations, assessment, development, and evaluation
HCP	healthcare provider
HHS	Department of Health and Human Services
IASP	International Association for the Study of Pain
IBD	Inflammatory Bowel Disease
ICPS	International Cannabis Policy Study
IND	investigational new drug
MD	Maryland
MMCC	Maryland Medical Cannabis Commission
MMCPs	Maryland Medical Cannabis Patient Survey
MN	Minnesota
MTF	Monitoring the Future

NAADAC	Association for Addiction Professionals
NASEM	National Academies of Sciences, Engineering, and Medicine
NDA	new drug application
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
NPDS	National Poison Data System
NRS	Numeric Rating Scale
NSDUH	National Survey on Drug Use and Health
OASH	Office of the Assistant Secretary for Health
OR	odds ratio
OSE	Office of Surveillance and Epidemiology
PDAS	public online data analysis system
PRISMA	preferred reporting items for systematic reviews and meta-analysis
PTSD	post-traumatic stress disorder
PUF	public use file
RCT	randomized controlled trials
RR	relative risk
RUF	restricted use file
SAE	serious adverse event
SAMHSA	Substance Abuse and Mental Health Services Administration
SAS	Statistical Analysis System
THC	tetrahydrocannabinol
UF	University of Florida
VAS	Visual Analog Scale

I. Executive Summary

1. Background

The Department of Health and Human Services (HHS) has conducted an evaluation of whether marijuana¹ has a "currently accepted medical use in treatment in the United States" (CAMU) for purposes of scheduling under the Controlled Substances Act (CSA), 21 U.S.C. 812(b). Such an evaluation is one of the findings relevant to the placement of a substance in one of five drug control "schedules" set forth in 21 U.S.C. 812(b).

In evaluating CAMU when considering whether to recommend rescheduling of marijuana, HHS applied a two-part test (hereinafter, "CAMU test") that takes into account the current widespread medical use of marijuana under the supervision of licensed health care practitioners (HCPs) under state-authorized programs. Under Part 1 of the CAMU test, the Office of the Assistant Secretary for Health (OASH) considered whether there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented state-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these state jurisdictions. Part 2 of the CAMU test, performed herein by the FDA, evaluates whether there exists some credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied. FDA's evaluation in Part 2 is not meant to be, nor is it, a determination of safety and efficacy that meets the Federal Food, Drug, and Cosmetic Act's (FD&C Act's) drug approval standard for new human or animal drugs. Rather, the two-part test is to determine whether a substance, in this case marijuana, has a CAMU for purposes of drug scheduling recommendations and placement in a drug schedule consistent with criteria set forth in 21 U.S.C. 812(b).

In the evaluation and assessment under Part 1 of the CAMU test, OASH found that more than 30,000 HCPs are authorized to recommend the use of marijuana for more than six million registered patients, constituting widespread clinical experience associated with various medical conditions recognized by a substantial number of jurisdictions across the United States. For several jurisdictions, these programs have been in place for several years, and include features that actively monitor medical use and product quality characteristics of marijuana dispensed. OASH, through the Assistant Secretary for Health, concluded that, taken together, the findings from Part 1 warrant an FDA assessment under Part 2 of the CAMU test to determine if there exists credible scientific support for the use of marijuana for at least one of the medical conditions identified by OASH under Part 1.

¹ See Section II.2.

FDA conducted Part 2 of the CAMU test for seven indications, based in part on OASH's findings under Part 1 of the CAMU test² and in part on FDA's own analysis of the landscape in which marijuana is currently used medically, including information from state-authorized programs on how and to what extent marijuana is being utilized for medical purposes. The seven indications are: anorexia³, anxiety⁴, epilepsy, inflammatory bowel disease (IBD), nausea and vomiting, pain, and post-traumatic stress disorder (PTSD). FDA's evaluation under Part 2 of the CAMU test was based on systematic reviews of studies investigating the safety and effectiveness of marijuana, relevant professional societies' position statements, data from state medical marijuana programs and U.S. national surveys, and the labeling of FDA-approved products relevant to the analysis.

2. Summary of Findings Under Part 2 of the CAMU Test

In evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors considered in favor of a positive finding included whether: 1) favorable clinical studies of the medical use of marijuana, although not necessarily adequate and well-controlled clinical studies that would support approval of a new drug application (NDA), have been published in peer-reviewed journals and/or 2) qualified expert organizations (e.g., academic or professional societies, government agencies) have opined in favor of the medical use or provided guidance to HCPs on the medical use. Factors considered that weigh against a finding that Part 2 of the CAMU test is met included whether: 1) data or information indicate that the medical use of the substance is associated with unacceptably high safety risks for the likely patient population, e.g., due to toxicity concerns; 2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; and/or 3) qualified expert organizations (e.g., academic or professional societies,

² In Part 1 of the CAMU test, OASH identified at least 15 medical conditions where there is widespread current experience with medical use of the substance in the United States by licensed health care practitioners operating in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine. These conditions include amyotrophic lateral sclerosis (ALS), autism, cachexia, cancer, chronic pain, Crohn's disease, epilepsy or condition causing seizures, glaucoma, HIV/AIDS, multiple sclerosis, Parkinson's disease, persistent/severe muscle spasm, persistent/severe nausea, PTSD, and spasticity. FDA conducted Part 2 of the analysis for the medical conditions identified by OASH that were likely to have the most robust evidence available for review; because our analysis concluded that the Part 2 test has been met for at least one of the conditions identified in Part 1, there was no need to analyze all of them.

³ The anorexia indication reflects anorexia due to a medical condition (e.g., HIV/AIDS) and does not represent anorexia nervosa.

⁴ While anxiety was not one of the specific medical conditions identified by OASH, it is included herein because anxiety was identified by the FDA during the Part 2 review of state-level usage data. See, e.g., Table 3. FDA considered the medical use of marijuana for the treatment of anxiety of importance to evaluate given the reported prevalence of marijuana use for the treatment of anxiety regardless of the legal status of such use in a given jurisdiction.

government agencies) recommend against the medical use of marijuana (based on the available data at the time of their position statement).

Our review of the available information identified mixed findings of effectiveness across indications, ranging from data showing inconclusive findings to considerable evidence in favor of effectiveness, depending on the source. The largest evidence base for effectiveness exists for marijuana use within the pain indication (in particular, neuropathic pain). For the pain indication, a systematic review of scientific and medical literature was conducted this year by the University of Florida (UF) (see Sections II.3.2 and II.4.2 for additional details) under contract with FDA. UF epidemiologists identified some data supporting effectiveness of marijuana, including some within their own meta-analysis; however, they ultimately concluded the results are inconclusive or mixed. FDA also conducted a separate review of published systematic reviews. Several of those reviews drew conclusions similar to UF. In contrast, numerous other systematic reviews concluded that there exists some level of evidence supporting the use of marijuana for painful conditions. Other reviews, such as the National Academies of Sciences, Engineering, and Medicine (NASEM) report (2017), concluded there was “substantial evidence”⁵ supporting the use of cannabis products relevant to this review for pain. The Agency for Healthcare Research and Quality’s (AHRQ) living systematic review has concluded that there is some support for the use of marijuana-related products in the treatment of pain, but overall concluded these effects were small and the increased risk of dizziness, nausea and sedation may limit the benefit.

UF evaluated other therapeutic conditions mentioned above, i.e., anorexia, anxiety, epilepsy, inflammatory bowel disease (IBD), nausea, and PTSD, employing a similar systematic review of scientific and medical literature. UF found that there is low- to moderate-quality evidence⁶ supporting the use of marijuana as medical treatment for outcomes in anorexia, nausea and vomiting, and PTSD. However, FDA review of systematic reviews showed mixed results for these indications. In particular, FDA found that the potential for psychiatric adverse events associated with treating PTSD with marijuana may be more substantial than any limited benefit in observational studies. Although UF did not conclude that there was evidence in support of the effectiveness of marijuana in IBD, both their review and other systematic reviews found some benefit with respect to subjective symptoms in this condition. With regard to epilepsy and anxiety, both UF’s review and FDA’s review of other systematic reviews did not find support for marijuana providing benefit in the treatment of these conditions. Where positive results on effectiveness outcome measures were found, the effects and the quality of evidence were generally in the low-to-moderate range. UF did not find high quality evidence supporting worsening of outcomes in any indication.

None of the evidence from the systematic reviews included in our CAMU Part 2 analysis identified any safety concerns that would preclude the use of marijuana in the indications

⁵ The term “substantial evidence” refers to language used within the NASEM report (2017) and is not meant to represent “substantial evidence” as defined in 21 USC 355(d).

⁶ UF determined the quality of evidence rating in accordance to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach described in the Cochrane handbook. For further details, please refer to the Section II.4.2.1 in this document.

for which there exists some credible scientific support for its therapeutic benefit. The clinical safety data identified in the literature from controlled trials were generally consistent between sources but limited in the rigor of safety reporting. The vast majority of the observational studies evaluated in the context of medical use were excluded from the final synthesis of evidence due to concerns regarding their quality (only one observational study for the anxiety indication and one for the PTSD indication were included). Generally, data on safety from both clinical trials and observational studies were scarce. Literature shows marijuana has more adverse events when compared to a placebo or active control group, however, typically in the mild to moderate severity range. Severe adverse events were uncommon.

FDA also reviewed results from state reporting data from 37 states with medical marijuana programs and surveys of patients using marijuana in Maryland and Minnesota, which had data available for review. Surveys of patients using marijuana in these two states found most patients did not report any side effects and those that did report side effects mostly described them as mild. Neither state's databases included patients who chose to stop using marijuana, which may result in an overestimation of positive experiences.

To date, real-world data sources available to FDA, in general, lack the necessary elements to identify the exposure (i.e., marijuana), to distinguish the reason for use (medical vs. recreational) and, if applicable, the condition that prompted its medical use, and/or to permit sound inferential analyses. Therefore, they were not included in this review.

Data from U.S. national surveys, in general, lacked details on patient characteristics and factors that prompted the use of marijuana for medical purposes, and data collection for these surveys was impacted by the coronavirus disease of 2019 (COVID-19) pandemic. Despite these limitations, these data suggested that medical use of marijuana increases as age increases. Only data from one survey provided information on intended indication for use, suggesting that users often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms, but only approximately half of them reportedly had ever asked a healthcare professional for a recommendation to use medical marijuana.

Additionally, although the safety data obtained from use in a medical context are considered to be the most relevant for the CAMU analysis, FDA evaluated the safety of marijuana in the nonmedical setting to inform the potential for more severe outcomes. Specifically, FDA evaluated safety outcomes related to marijuana use in the setting of nonmedical use, use of uncertain intent, and unintentional exposure through a variety of epidemiological data sources and in relation to several comparator substances controlled under the CSA, including drugs in Schedule I: heroin (an illicit opioid drug); Schedule II: hydrocodone and oxycodone (approved opioid prescription drugs), cocaine and fentanyl (largely illicitly produced drugs in the nonmedical use setting, although there are approved prescription drugs); Schedule III: ketamine (an approved prescription drug); and Schedule IV: zolpidem, benzodiazepines, and tramadol (approved prescription drugs) ([FDA Office of Surveillance and Epidemiology, 2023](#)). The comparative data demonstrate that, even in the context of nonmedical use, marijuana has a less concerning

overall safety profile relative to the comparators for a number of important outcomes (e.g., single substance use overdose death, hospitalizations). However, in young children, population-adjusted rates of emergency department visits and hospitalizations involving marijuana poisoning were higher than heroin, cocaine, and benzodiazepines for the periods studied. Of note, some of the comparator substances are approved for use in conditions similar to the indications for which marijuana is being evaluated in this CAMU analysis (e.g., opioids for pain, benzodiazepines for anxiety related conditions).

FDA also considered position statements from professional organizations relevant to the indications discussed. The vast majority of professional organizations did not recommend the medical use of marijuana in their respective specialty; however, none specifically recommended against it, with the exception of the American Psychiatric Association (APA), which stated that marijuana is known to worsen certain psychiatric conditions.

On balance, the available data indicate that there is some credible scientific support for the use of marijuana in the treatment of pain, anorexia, and nausea and vomiting (e.g., chemotherapy-induced), with varying degrees of support and consistency of findings. Additionally, no safety concerns were identified in our review that would indicate that medical use of marijuana poses unacceptably high safety risks for the indications where there is some credible scientific evidence supporting its therapeutic use.

3. Conclusions on Marijuana and CAMU

Based on the totality of the available data, we conclude that there exists some credible scientific support for the medical use of marijuana in at least one of the indications for which there is widespread current experience in the United States, as identified by OASH under Part 1 of the CAMU test. Seven indications were selected for evaluation under Part 2 of the CAMU test based on conclusions from Part 1 of the CAMU test as well as the FDA's analysis of the landscape of medical use of marijuana. The indications evaluated included anorexia related to a medical condition, anxiety, epilepsy, inflammatory bowel disease, nausea and vomiting (e.g., chemotherapy-induced), pain, and post-traumatic stress disorder. The analysis and conclusions on the available data are not meant to imply that safety and effectiveness have been established for marijuana that would support FDA approval of a marijuana drug product for a particular indication. However, the available data do provide some level of support for the way marijuana is being used in clinical practice. Thus, based on the widespread HCP experience and the extent of medical use evaluated by OASH under the Part 1 test, and an evaluation of available credible scientific support described herein for at least some therapeutic uses identified in the Part 1 test, we find that, for purposes of the drug scheduling criteria in 21 U.S.C. 812(b), marijuana has a currently accepted medical use in the United States for: anorexia related to a medical condition; nausea and vomiting (e.g., chemotherapy-induced); and pain.

II. Evaluation of Marijuana with Respect to CAMU

1. Introduction

Drugs or other substances with abuse potential are placed into one of five schedules (i.e., Schedule I, II, III, IV, or V) under the federal Controlled Substances Act (CSA) based on whether the drug has a currently accepted medical use in treatment in the United States and its degree of abuse and dependency potential. Collectively, drugs and other substances listed among the five drug schedules are controlled substances under federal law and are subject to the federal regulatory requirements of the Drug Enforcement Administration (DEA), where regulatory requirements may vary relative to each of the five drug control schedules. Stricter regulatory controls are associated with schedules that are for those substances posing the greatest harms to public health, i.e., substances controlled under Schedule I and II which have a high potential for abuse and greatest safety concerns and potential to cause severe psychological and/or physical dependence. Specifically, drugs controlled under Schedule I have a high potential for abuse but do not have a currently accepted medical use, whereas drugs controlled under Schedule II have the same high potential for abuse but have a currently accepted medical use in treatment in the United States (CAMU) or a currently accepted medical use with severe restrictions. Drugs in Schedule III, IV, and V, have a currently accepted medical use, but substances in these schedules have incrementally decreasing degrees of abuse potential and dependence liability, i.e., Schedule V having substances with the lowest abuse potential and dependence liability while still warranting some degree of regulatory controls.

On October 6, 2022, the Biden Administration issued a statement on reforms associated with marijuana,⁷ a substance currently controlled in Schedule I of the CSA ([Biden 2022](#)). As part of the statement, the President directed the Secretary of the Department of Health and Human Services (HHS) and the Attorney General to initiate the administrative process to review expeditiously how marijuana is scheduled under federal law. The Secretary requested that the FDA, in consultation with the National Institute on Drug Abuse (NIDA), conduct a scientific and medical evaluation of marijuana that would enable the Office of the Assistant Secretary for Health (OASH), on behalf of the Secretary, to convey recommendations to the DEA regarding the appropriate scheduling of marijuana. A necessary component of the overall scientific and medical evaluation of marijuana for drug scheduling purposes is a finding as to whether marijuana is considered to have a CAMU in the United States under the CSA, where such finding will have implications for the schedule of control that is ultimately recommended by HHS as most appropriate in accordance with 21 U.S.C. 812(b). This document is intended to analyze and present the relevant data and make a determination as to whether marijuana is considered to have a CAMU in the United States under the CSA.

The approach for evaluating CAMU in this memo is a two-part test (hereafter referred to as “CAMU test”). To satisfy Part 1 of the CAMU test, there must be widespread current experience with medical use of the substance in the United States by licensed health care

⁷ “Marijuana” as defined in 21 U.S.C. 802(16)

practitioners operating in accordance with implemented state-authorized programs, where medical use is recognized by entities that regulate the practice of medicine. To satisfy Part 2 of the CAMU test, there must exist some credible scientific support for a least one of the medical uses for which Part 1 of the CAMU test has been met. The purpose of this test is not to determine that the substance is safe and effective under the FD&C Act's drug approval standard, but rather to determine whether there is some credible scientific support for at least one medical use of the substance for which Part 1 of the CAMU test is satisfied, in order to determine whether there is a CAMU for purposes of drug scheduling recommendations under the administrative drug scheduling process [21 U.S.C. 811(a-c) and 812(b)].

2. Definitions Relevant to the Analysis of Whether Marijuana Has a CAMU

Marijuana is a psychoactive drug produced from the *Cannabis sativa* L. plant. Cannabis is one of the oldest cultivated crops, providing a source of fiber, food, oil, and drug, and it contains a variety of chemical compounds, including delta-9-tetrahydrocannabinol (Δ 9-THC). Δ 9-THC is considered to be the main psychoactive component of the *Cannabis sativa* L. plant; however, the plant is also known to contain other psychoactive cannabinoids.

Marijuana is a subset of cannabis, and the CSA defines marijuana or "marihuana"⁸ as:

(16)(A) Subject to subparagraph (B), the terms "marihuana" and "marijuana" mean all parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.

(B) The terms "marihuana" and "marijuana" do not include-

(i) hemp, as defined in section 1639o of title 7; or

(ii) the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.

The exclusion of "hemp"-type cannabis from marijuana's Schedule I control status reflects the provisions of the 2018 Agriculture Improvement Act (i.e., the "Farm Bill"), which defined hemp as *Cannabis sativa* L. and its derivatives with no more than 0.3 percent Δ 9-THC on a dry weight basis, and explicitly revised the definition of marijuana in the CSA to exclude, and effectively decontrol, hemp.

⁸ 21 U.S.C. 802(16)

As this document is evaluating the CAMU for marijuana, as it is defined and controlled under Schedule I of the CSA, we will use the term marijuana for our analysis. However, when describing information referenced from other sources, our language will reflect the terminology used in those sources. Additionally, for the purposes of this review, we will use Δ9-THC and THC interchangeably.

3. Overview of the Analysis of Marijuana and CAMU: Parts 1 and 2

3.1. Summary of the OASH Findings Under Part 1 of the CAMU Test

To determine whether marijuana has a CAMU in the United States, OASH conducted an analysis consisting of the first component of the aforementioned two-part test. The goal of Part 1 was to identify whether widespread, current experience with marijuana exists for at least one medical use within jurisdiction-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine. Support for satisfying Part 1 was based on any of the following factors: the number of licensed HCPs who have gained clinical experience with marijuana in at least one specific medical use; the number of entities that regulate the practice of medicine recognize at least one medical use of marijuana and its extent; and the duration of HCP experience with prescribing marijuana for medical use.

OASH conducted the evaluation and assessment of marijuana under Part 1 of the CAMU test and has confirmed that more than 30,000 HCPs across 43 U.S. jurisdictions are authorized to recommend the medical use of marijuana for more than six million legally registered patients for at least 15 medical conditions. Taken together, the data support that a substantial number of HCPs have gained clinical experience with marijuana, and a substantial number of regulatory entities recognize at least one specific medical use of marijuana under authorized programs. Additionally, OASH concluded that HCPs' clinical experience with the use of marijuana for various medical conditions is of sufficient extent and duration to help evaluate potential clinical uses. OASH further noted, however, that based on the available secondary data for this analysis, it could not be conclusively determined whether HCP clinical experience with the use of marijuana is of sufficient extent and duration to help evaluate the longer-term toxicities and potential harms of marijuana when used under medical supervision.

OASH, through the Assistant Secretary for Health, concluded that “the findings from Part 1 warrant an FDA assessment under Part 2 of the Department’s CAMU approach to determine if there exists credible scientific support for the use of marijuana for at least one of the medical conditions [identified by OASH under Part 1].”

3.2. Approach to Part 2 of the CAMU Test

To satisfy Part 2 of the CAMU test, there must exist some credible scientific support for at least one of the medical uses for which Part 1 of the CAMU test has been met. In

evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors considered in favor of a positive finding included whether 1) favorable clinical studies of the medical use of marijuana, although not necessarily adequate and well-controlled clinical studies that would support FDA approval of a new drug application (NDA), have been published in peer-reviewed journals, and/or 2) qualified expert organizations (e.g., academic or professional societies, government agencies) have opined in favor of the medical use or provided guidance to HCPs on the medical use. Factors considered that weigh against a finding that Part 2 of the CAMU test is met included whether: 1) data or information indicate that the medical use of marijuana is associated with unacceptably high safety risks for the likely patient population, e.g., due to toxicity concerns; 2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; and/or 3) qualified expert organizations (e.g., academic or professional societies, government agencies) have recommended against the medical use of marijuana.

To evaluate marijuana under Part 2 of the CAMU test, this memo will consider data from peer-reviewed publications included in a systematic review of the medical literature on marijuana that was conducted by the Consortium for Medical Marijuana Clinical Outcomes Research at the University of Florida (hereafter referred to as the “University of Florida” or “UF”), a review of published systematic reviews, analysis of safety data that have been collected through state medical marijuana programs, data on patterns of use in the context of medical use as reported in U.S. national surveys, FDA’s findings for approved drug products related to marijuana (e.g., Marinol), and expert opinions and position statements from professional organizations. Examples of meeting the requirement for demonstrating some credible scientific support would be peer-reviewed clinical studies reporting evidence of benefit, or a reputable medical/scientific organization recommending treatment with marijuana for an indication within their area of expertise. The overall conclusions on the criteria for Part 2 of the CAMU test will be based on the totality of the available evidence described above.

4. Assessment of Data Under Part 2 of the CAMU Test for Marijuana

4.1. Patterns of Use in the Context of Medical Use

The purpose of this section is to describe the patterns of medical use of marijuana as reported in U.S. national surveys. Thus, FDA examined patterns of use among medical users of marijuana as reported in four U.S. national surveys: The International Cannabis Policy Study (ICPS), Substance Abuse and Mental Health Services Administration (SAMHSA)’s National Survey on Drug Use and Health (NSDUH), the Centers for Disease Control and Prevention (CDC)’s Behavioral Risk Factor Surveillance System (BRFSS), and the National Institute for Drug Abuse (NIDA)’s Monitoring the Future (MTF).

4.1.1. International Cannabis Policy Study (ICPS)

4.1.1.1. Methods

The ICPS is an international research collaboration led by the University of Waterloo, Canada, designed to examine the public health impact of cannabis legalization in the United States. The ICPS Project includes national population-based surveys conducted annually in the United States since 2018 via self-completed web-based surveys using a repeat cross-sectional design. ICPS recruited individuals through the Nielsen Consumer Insights Global Panel and their partners' panels using non-probability sampling methods. After targeting for age and country criteria, ICPS sent email invitations (with a unique link) to a random sample of panelists (panelists known to be ineligible were not invited).⁹ ICPS oversampled individuals from states that had legalized 'non-medical adult' cannabis in order to provide more robust estimates for individual states. Individuals were eligible to participate in the survey if they resided in the United States, were 16-65 years of age at the time of recruitment and had access to the internet. Respondents were provided with information about the study and provided consent prior to completing the survey for which they received remuneration.

ICPS assessed medical versus 'non-medical' or recreational use among past 12-month cannabis consumers beginning in the 2019 ICPS surveys, and modified the measure in 2020 and 2021 to capture exclusive vs. non-exclusive medical use.¹⁰ ICPS conducted all analyses using post-stratification weights constructed based on the U.S. census estimates. ICPS reported frequencies and descriptive statistics with 95% confidence intervals.¹¹ Analyses are presented based on the legal status of marijuana at the state-level based on three categories: 'recreational states' (states that have legalized adult 'non-medical' marijuana), 'medical states' (states that have legalized medical marijuana, but not 'non-medical' marijuana use), and 'illegal states' (states in which neither 'medical' nor 'non-medical' marijuana use has been legalized at the state level) [Appendix Table 55 for calendar year 2021]. The University of Waterloo conducted all analyses using survey procedures in Statistical Analysis System [SAS] (SAS version 9.4, SAS Institute Inc., Cary, NC, USA). Technical reports for the ICPS surveys provide additional methodological description and are publicly accessible ([Corsetti et al. 2022](#)).

⁹ Individuals outside of the age range (<16 and >65 years), any panelists that resided outside the United States, or those that do not speak English.

¹⁰ The question wording was modified using a 'split half' approach, in which half of respondents in the 2020 and 2021 survey were asked the question using the original 2019 wording (i.e., "Do you self-identify as a medical marijuana user only?"), and half were asked the modified question wording (i.e., "Do you self-identify as a medical marijuana user?").

¹¹ Any estimates based on less than 30 respondents should be interpreted with caution.

4.1.1.2. Results

ICPS collected data from a total of 107,572 respondents aged 16-65 years between 2018 and 2021. The response rate was 64.2% in 2018, 62.9% in 2019, 62.0% in 2020, and 60.8% in 2021. Overall, across the four cohorts, the sample had a similar sex distribution, with approximately 60% of individuals ages 45-64 years, a majority of non-Hispanic and White people, most with some college education or a bachelor's degree, and similarly distributed in regard to income adequacy.¹² Approximately 50% of the sample reported having ever consumed cannabis for any reason (Appendix Table 56).

A total of 60,193 individuals (56% of 107,572 respondents) were asked whether they identified themselves as a user of cannabis exclusively for medical reasons in the year prior. Approximately 8-10% of this subset of the sample reported being a user of cannabis in the past year for medical reasons only (exclusive) while approximately 20% reported other (recreational) use (Table 1).

Table 1. Reason for Past-Year Use of Cannabis, ICPS, 2018-2021

Reason for Past-Year Use	2018 ² N/A	2019 ³ (n=30,366)	2020 ⁴ (n=14,762)	2021 ⁵ (n=14,858)
Medical use (exclusive) ¹	N/A	8.9% (2,712) (8.4% - 9.4%)	7.9% (1,170) (7.5% - 8.4%)	9.7% (1,447) (9.3% - 10.2%)
Other ('recreational')	N/A	21.7% (6,598) (21.0% - 22.4%)	19.1% (2,819) (18.5% - 19.7%)	22.0% (3,265) (21.3% - 22.7%)

Source: (Hammond et al. 2023), Table 2a

¹ Respondents were asked "Do you self-identify as a medical marijuana user only?" ('exclusive' medical use)

² In 2018, respondents were not asked if they self-identify as a medical cannabis consumer.

³ In 2019, 94 responses were excluded for refusal to answer

⁴ In 2020 the denominator only includes those who would have seen the 'split half version of the question specific to exclusive medical use; 71 responses excluded for refusal to answer.

⁵ In 2021 the denominator only includes those who would have seen the 'split half version of the question specific to exclusive medical use; 42 responses excluded for refusal to answer.

In the 2021 survey, among the 1,447 individuals reporting cannabis use exclusively for medical reasons in the past year, 56.8% (95% CI [confidence interval]: 53.0% - 60.7%) reported ever having asked a licensed health professional for a recommendation to use medical cannabis (Table 2). This prevalence rate appears to be only slightly impacted by the legal status of marijuana in the state of residence as 47% (95% CI: 38.6% - 55.4%) of users residing in states with illegal status asked their providers for a prescription/authorization to use medical cannabis.

¹² The wording of the question was "Thinking about your family's income, how difficult or easy is it to make ends meet? 'Making ends meet' means having enough money to pay for the thing your family needs."

Table 2. Ever Asked a Licensed Health Professional for a Recommendation to Use Medical Cannabis, Among Exclusive Past-Year Medical Cannabis Consumers, 2021

Response	Medical (Exclusive)			All States (n=1,447)
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	
Yes	47.0% (165) (38.6% - 55.4%)	60.2% (271) (53.3% - 67.0%)	59.9% (387) (54.3% - 65.5%)	56.8% (822) (53.0% - 60.7%)
No	50.1% (176) (41.6% - 58.5%)	37.9% (170) (31.0% - 44.7%)	37.7% (244) (32.2% - 43.3%)	40.8% (590) (36.9% - 44.6%)
Missing ¹	3.0% (10) (0.1% - 5.8%)	2.0% (9) (0.0% - 3.9%)	2.4% (15) (1.2% - 3.6%)	2.4% (35) (1.3% - 3.4%)

Source: (Hammond et al. 2023), Table 95.

¹ "Missing" includes respondents who responded "Don't know" or refused to answer.

Most (67.4%; 95% CI: 63.6-71.1) participants reporting exclusive medical use of cannabis used cannabis in the past month, without significant differences driven by state legal status. Time since last use of cannabis by sex, age group, race, and ethnicity, overall and by state legal status, is shown in the Appendix (Table 57, Table 58, Table 59, and Table 60).

Approximately 86.7% (n=1,255) of exclusive medical users reported ever using cannabis to improve or manage symptoms related to at least one psychiatric condition. The most frequent selected conditions included anxiety (67.3%), depression (47.8%), post-traumatic stress disorder [PTSD] (31.2%), bipolar disorder (17.2%), and alcohol or other drug use (9.8%) (Table 3).

Table 3. Ever-Use of Cannabis to Improve or Manage Symptoms for Any of the Selected Psychiatric Conditions, Among Exclusive Past-Year Medical Cannabis Consumers, 2021

Symptom	Medical (Exclusive) ¹			All States (n=1,447)
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	
Anxiety	69.6% (244) (61.9% - 77.2%)	68.6% (309) (62.1% - 75.1%)	65.3% (422) (60.0% - 70.5%)	67.3% (974) (63.7% - 70.9%)
Depression	55.4% (194) (47.0% - 63.8%)	53.4% (240) (46.5% - 60.3%)	39.7% (257) (34.0% - 45.4%)	47.8% (691) (43.9% - 51.7%)
PTSD	39.8% (140) (31.7% - 48.0%)	29.0% (131) (23.2% - 34.9%)	28.1% (181) (23.0% - 33.2%)	31.2% (452) (27.7% - 34.8%)
Bipolar disorder	25.6% (90) (18.2% - 33.0%)	13.4% (60) (9.3% - 17.5%)	15.4% (99) (11.5% - 19.3%)	17.2% (249) (14.4% - 20.1%)
Psychosis	8.0% (28) (3.0% - 13.1%)	9.3% (42) (5.0% - 13.6%)	8.2% (53) (5.1% - 11.4%)	8.5% (123) (6.2% - 10.8%)
Schizophrenia	5.5% (19) (1.1% - 9.8%)	5.9% (27) (2.6% - 9.3%)	2.1% (14) (1.2% - 3.1%)	4.1% (60) (2.6% - 5.7%)
Alcohol or other drug use	9.4% (33) (4.3% - 14.5%)	10.7% (48) (6.3% - 15.1%)	8.5% (55) (5.2% - 11.7%)	9.4% (136) (7.0% - 11.7%)
Eating disorder	9.5% (33) (4.6% - 14.4%)	7.4% (33) (4.0% - 10.8%)	8.8% (57) (5.8% - 11.8%)	8.5% (124) (6.5% - 10.6%)
ADD/ADHD	8.9% (31) (3.9% - 13.8%)	10.3% (46) (6.4% - 14.2%)	9.9% (64) (6.8% - 13.0%)	9.8% (141) (7.6% - 12.0%)
Other	0.0% (0) (0.0% - 0.0%)	0.5% (2) (0.0% - 1.1%)	0.4% (2) (0.1% - 0.7%)	0.3% (5) (0.1% - 0.6%)

Symptom	Medical (Exclusive) ¹			All States (n=1,447)
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	
None	5.9% (21) (2.9% - 8.9%)	12.5% (56) (8.0% - 17.0%)	17.8% (115) (13.2% - 22.3%)	13.3% (192) (10.6% - 15.9%)
Missing ²	1.8% (6) (0.0% - 4.7%)	3.4% (15) (0.5% - 6.4%)	1.7% (11) (0.9% - 2.5%)	2.3% (33) (1.1% - 3.5%)

Source: (Hammond et al. 2023), Table 10b.

¹ Response options are not mutually exclusive options, column total may sum to greater than 100%.² "Missing" includes respondents who responded "Don't know" or refused to answer.

Exclusive medical cannabis consumers also often reported use of cannabis to improve or manage symptoms of pain (59.7%), headaches and migraines (48.0%), problems sleeping (39.3%), lack of appetite (27.1%), nausea or vomiting or chemotherapy symptoms (24.6%), and muscle spasms (22.1%) (Table 4).

Table 4. Ever-Use of Cannabis to Improve or Manage Symptoms for Any of the Following, Among Exclusive Past-Year Medical Cannabis Consumers, 2021

Symptom	Medical (Exclusive) ¹			All States (n=1,447)
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	
Headaches/migraines	51.4% (180) (43.0% - 59.9%)	47.8% (215) (40.9% - 54.7%)	46.4% (300) (40.5% - 52.2%)	48.0% (695) (44.1% - 52.0%)
Pain	64.2% (225) (56.0% - 72.5%)	56.5% (254) (49.5% - 63.4%)	59.6% (385) (53.8% - 65.3%)	59.7% (864) (55.8% - 63.6%)
Nausea/vomiting or chemotherapy symptoms	30.6% (107) (23.2% - 37.9%)	23.2% (104) (17.4% - 28.9%)	22.5% (145) (17.9% - 27.1%)	24.6% (357) (21.4% - 27.9%)
Lack of appetite	30.5% (107) (22.6% - 38.4%)	24.5% (110) (18.6% - 30.5%)	27.0% (174) (21.5% - 32.4%)	27.1% (392) (23.5% - 30.7%)
Seizures	13.5% (47) (6.4% - 20.6%)	7.3% (33) (3.4% - 11.2%)	4.6% (30) (3.1% - 6.1%)	7.6% (110) (5.4% - 9.9%)
Muscle spasms	20.7% (73) (13.9% - 27.5%)	21.1% (95) (15.6% - 26.6%)	23.6% (152) (18.7% - 28.4%)	22.1% (320) (18.9% - 25.3%)
To shrink tumors or treat cancer	5.5% (19) (1.1% - 10.0%)	4.5% (20) (1.5% - 7.5%)	3.6% (23) (2.0% - 5.3%)	4.4% (63) (2.8% - 6.0%)
Problems sleeping	44.0% (154) (35.8% - 52.3%)	38.2% (172) (31.7% - 44.7%)	37.6% (243) (32.0% - 43.1%)	39.3% (569) (35.6% - 43.1%)
Digestion/gastrointestinal issues	17.6% (62) (10.5% - 24.7%)	12.2% (55) (8.0% - 16.4%)	14.6% (94) (10.2% - 19.0%)	14.6% (211) (11.6% - 17.5%)
Fibromyalgia	8.5% (30) (4.9% - 12.0%)	10.0% (45) (6.4% - 13.6%)	6.5% (42) (4.8% - 8.2%)	8.1% (117) (6.4% - 9.7%)
None	3.7% (13) (0.7% - 6.8%)	4.0% (18) (1.0% - 7.1%)	3.2% (20) (1.3% - 5.0%)	3.6% (52) (2.1% - 5.0%)
Missing ²	2.3% (8) (0.0% - 5.3%)	2.7% (12) (0.0% - 5.5%)	1.3% (9) (0.5% - 2.1%)	2.0% (29) (0.8% - 3.2%)

Source: (Hammond et al. 2023), Table 10b.

¹ Response options are not mutually exclusive options, column total may sum to greater than 100%.² "Missing" includes respondents who responded "Don't know" or refused to answer.

Although 34.1% of respondents did not provide an answer, 60.5% of those who reported use of cannabis exclusively for medical reasons in the past year reported having used cannabis for pain relief, instead of using opioids or prescription pain medication in the past 12 months (Table 5).

Table 5. Used Cannabis for Pain Relief, Instead of Using Opioids or Prescription Pain Medication in the Past 12 Months, Among Exclusive Past-Year Medical Cannabis Consumers, 2021

Response	Medical (Exclusive)			
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	All States (n=1,447)
Yes	62.1% (218) (53.9% - 70.6%)	58.7% (264) (51.7% - 65.6%)	61.0% (393) (55.3% - 66.6%)	60.5% (876) (56.7% - 64.4%)
No	8.3% (29) (3.2% - 13.0%)	4.7% (21) (1.6% - 7.6%)	4.3% (28) (2.5% - 6.1%)	5.3% (77) (3.6% - 7.0%)
Missing ¹	29.6% (104) (21.7% - 37.5%)	36.7% (165) (29.9% - 43.6%)	34.8% (225) (29.2% - 40.4%)	34.1% (494) (30.3% - 37.9%)

Source: (Hammond et al. 2023), Table 110.

¹ "Missing" includes respondents who responded "Don't know" or refused to answer.

At least 40% of exclusive medical users reported using cannabis and alcohol simultaneously, with approximately 11.7% of individuals reporting often or always consuming both substances together (Table 6).

Table 6. Past-Year Co-Use of Alcohol With Cannabis Among Exclusive Past-Year Medical Cannabis Consumers, 2021

Frequency	Medical (Exclusive) ^{1,2}			
	'Illegal' States (n=351)	'Medical' States (n=450)	'Recreational' States (n=646)	All States (n=1,447)
Never ³	59.3% (208) (50.9% - 67.6%)	55.7% (251) (48.8% - 62.6%)	56.2% (363) (50.3% - 62.0%)	56.8% (821) (52.8% - 60.7%)
Sometimes	24.1% (84) (17.2% - 30.9%)	29.9% (134) (23.5% - 36.2%)	32.8% (212) (27.1% - 38.6%)	29.8% (431) (26.1% - 33.4%)
Often	10.8% (38) (4.9% - 16.7%)	6.6% (30) (3.1% - 10.2%)	7.6% (49) (5.2% - 9.9%)	8.1% (117) (6.0% - 10.2%)
Every time I use cannabis	5.9% (21) (1.0% - 10.7%)	4.4% (20) (1.4% - 7.5%)	1.9% (12) (0.5% - 3.3%)	3.6% (53) (2.0% - 5.3%)

Source: (Hammond et al. 2023), Table 91.

¹ This question was asked only to respondents who had used cannabis in the past 12 months and ever used alcohol.² "Don't know" responses are not shown in the table: 'medical states' n=15; 'recreational states' n=10; 'all states' n=25.³ Those who never used alcohol were included in the "Never" category for this table.

Past-year users of cannabis exclusively for medical purposes more often reported obtaining cannabis from stores/dispensaries (49.7%), followed by family/friends (44.7%), and dealers, while 18.6% reported growing cannabis or making their own cannabis products (Appendix Table 61). Among those reporting purchasing cannabis from a store, approximately 6.3% reported sourcing their cannabis from an illegal/unauthorized store (Appendix Table 62).

4.1.1.3. Discussion

FDA primarily summarized findings among the 1,447 users of cannabis ages 16–65 years surveyed in 2021 who self-reported exclusive use for medical reasons in the past 12 months. Most (67.1%) of these individuals reported use in the past month. Slightly more than half reported ever asking a licensed health professional for a recommendation to use medical cannabis, with slightly higher levels in states that had legalized medical or recreational marijuana. Approximately 86.7% of medical users reported using cannabis to improve or manage psychiatric symptoms, most commonly for depression, anxiety and

PTSD. Medical cannabis users also often reported using cannabis to manage pain, followed by headaches or migraines, sleep disorders, to manage nausea and vomiting, lack of appetite, and muscle spasms. At least 40% of individuals reported using cannabis and alcohol simultaneously. Medical users reported obtaining cannabis through different sources with stores and dispensaries being the most commonly reported cannabis source, followed by family and friends, and dealers. Approximately 19% reported growing cannabis or making their own cannabis products.

These analyses are subject to the limited sample of self-identified exclusive medical users as well as to limitations inherent to survey research, which include the cross-sectional nature of the data and potential for response bias. Self-reported measures of cannabis use are subject to social desirability bias, including for prevalence of use and measures such as purchasing cannabis from illegal retail sources. ICPS recruited respondents using non-probability-based sampling; therefore, the findings do not necessarily provide nationally representative estimates. Lastly, ICPS did not restrict to marijuana in their questions, therefore, to some extent, respondents might have been referring to cannabis-derived products instead that are legal at the federal level (i.e., hemp as defined by the 2018 Farm Bill) as both terms are often used interchangeably.

4.1.2. National Survey on Drug Use and Health (NSDUH)

4.1.2.1. Methods

The NSDUH is an annual, nationally representative, cross-sectional household survey of individuals ages 12 and older that provides information on the use of prescription and illicit drugs in the United States. Since 2015, NSDUH has elicited information on any use, as well as nonmedical use (abuse or misuse), of select prescription and illicit drugs in the past year.

FDA used data from SAMHSA's public online data analysis system (PDAS) to analyze public use data from 2015 to 2020 ([SAMHSA 2023](#)). FDA requested that SAMHSA conduct custom analyses of 2021 using the restricted use file (RUF) rather than the public use file. Due to disclosure avoidance methods used in creating the public use file (PUF), national estimates in terms of numbers and percent may differ between sources; however, disclosure methods have been implemented in such a way that the PUF continues to be representative of civilian members of the noninstitutionalized population in the United States ([CBHSQ 2022b](#)). FDA reported national estimates in terms of numbers of individuals, percent of the total population, and percent of people with any past-year or past-month as well as use as per health care provider recommendation. Additional details are described elsewhere ([FDA Office of Surveillance and Epidemiology, 2023](#)).

4.1.2.2. Results

The weighted sample included a total of 267,694,489 individuals ages 12 years and older in 2015; 269,430,135 in 2016; 272,103,335 in 2017; 273,753,043 in 2018; 275,221,248 in 2019; 276,911,975 in 2020; and 279,843,944 in 2021. The prevalence in use of

marijuana (any use) in the past year ranged from 13.6% in 2015 to 18.7% in 2021 (FDA Office of Surveillance and Epidemiology, 2023).

The use of marijuana was not recommended by a healthcare provider for the large majority (>84.2%) of participants who reported its use in the year prior (Table 7). The percent of individuals who used marijuana only for the reason for which it was recommended to them by an HCP ranged from 6.8% to 10.0%. An additional 3.6% to 5.8% of respondents had an HCP recommendation but also used it for nonmedical purposes (Table 7).

Table 7. Marijuana Use Recommended by a Healthcare Provider, Individuals Ages 12 Years or Older With Past-Year Use of Marijuana: National Survey on Drug Use and Health, 2015-2021 (Numbers in Thousands)

Year	Nonmedical Use Only: No Recommendation by Healthcare Provider	Medical Use Only: Use as Per Recommendation by Healthcare Provider	Both Medical and Nonmedical Use: Some Use as Per Recommendation by Healthcare Provider
	Weighted Frequency in Thousands (%)	Weighted Frequency in Thousands (%)	Weighted Frequency in Thousands (%)
2015	32,027 (89.0%)	2,631 (7.3%)	1,344 (3.7%)
2016	32,951 (88.6%)	2,907 (7.8%)	1,341 (3.6%)
2017	35,934 (89.0%)	2,745 (6.8%)	1,716 (4.3%)
2018	38,024 (87.9%)	3,312 (7.7%)	1,913 (4.5%)
2019	41,897 (87.5%)	3,723 (7.8%)	2,292 (4.8%)
2020	40,064 (84.2%)	4,746 (10.0%)	2,751 (5.8%)
2021	43,784 (85.8%)	4,502 (8.8%)	2,750 (5.4%)

Source: 2015-2020 provided using NSDUH Public Data Analysis System (PDAS) system analysis of Public Use File (SAMHSA 2023). 2021 estimates provided using custom SAMHSA analysis of Restricted Use File (BRISQ 2022).
Note: Analysis excluded under 1% of observations with values coded as "bad data" (i.e., usually inconsistent with other data). People who used marijuana in the past year but did not specify whether their use was recommended by a doctor or other healthcare professional were excluded.
Data cited at (FDA Office of Surveillance and Epidemiology, 2023), Table 3.1.1.

Nearly all adolescents who used marijuana did not have an HCP recommendation (Table 8). Individuals ages 35-64 and 65+ years appeared to be more likely to have used marijuana only under an HCP recommendation in the year prior than the younger age groups. As such, in 2021, 97.0% of individuals ages 12-17 years with past-year use of marijuana reported use without a recommendation by their HCP, with only 1.0% of individuals reporting use exclusively as per HCP recommendation and an additional 1.9% reporting some use of marijuana as per HCP recommendation and some use for other reasons. For the same year, 83.7% of individuals ages 65+ years with past-year use of marijuana reported use without a recommendation by their HCP, with 11.6% of individuals reporting use exclusively as per HCP recommendation and an additional 4.7% reporting some use of marijuana as per HCP recommendation and some use for other reasons.

Table 8. Marijuana Use Recommended by a Healthcare Provider, Individuals Ages 12 Years or Older With Past-Year Use of Marijuana by Age Group: National Survey on Drug Use and Health, 2015-2021 (Numbers in Thousands)

Year	12-17 Years Weighted Frequency in Thousands (%)	18-25 Years Weighted Frequency in Thousands (%)	26-34 Years Weighted Frequency in Thousands (%)	35-64 Years Weighted Frequency in Thousands (%)	65+ Years Weighted Frequency in Thousands (%)
Nonmedical Use Only: No Recommendation by Healthcare Provider					
2015	2,950 (97.3%)	10,370 (91.8%)	7,091 (88.4%)	10,773 (86.0%)	843 (74.8%)
2016	2,773 (96.4%)	10,350 (91.9%)	7,683 (88.2%)	10,945 (85.3%)	1,199 (78.8%)
2017	2,949 (97.1%)	10,852 (92.0%)	7,956 (87.5%)	12,703 (86.6%)	1,476 (81.7%)
2018	2,918 (96.7%)	10,826 (92.1%)	8,934 (86.7%)	13,588 (84.6%)	1,758 (82.7%)
2019	3,105 (96.7%)	10,811 (91.6%)	10,147 (88.4%)	15,694 (83.6%)	2,140 (81.0%)
2020	2,286 (96.2%)	10,480 (90.9%)	9,339 (86.4%)	15,460 (78.6%)	2,498 (78.9%)
2021	2,414 (97.0%)	10,345 (90.6%)	10,376 (85.6%)	17,455 (82.3%)	3,194 (83.7%)
Medical Use Only: Use as Per Recommendation by Healthcare Provider					
2015	21 (0.7%)	522 (4.6%)	653 (8.1%)	1,196 (9.5%)	240 (21.3%)
2016	31 (1.1%)	530 (4.7%)	625 (7.2%)	1,461 (11.4%)	260 (17.1%)
2017	34 (1.1%)	484 (4.1%)	692 (7.6%)	1,270 (8.7%)	264 (14.6%)
2018	34 (1.1%)	464 (4.0%)	881 (8.6%)	1,681 (10.5%)	252 (11.9%)
2019	37 (1.2%)	510 (4.3%)	707 (6.2%)	2,171 (11.6%)	298 (11.3%)
2020	62 (2.6%)	487 (4.2%)	852 (7.9%)	2,849 (14.5%)	496 (15.7%)
2021	25 (1.0%)	553 (4.8%)	1,019 (8.4%)	2,463 (11.6%)	441 (11.6%)
Both Medical and Nonmedical Use: Some Use as Per Recommendation by Healthcare Provider					
2015	62 (2.0%)	401 (3.5%)	282 (3.5%)	556 (4.4%)	44 (3.9%)
2016	74 (2.6%)	379 (3.4%)	401 (4.6%)	423 (3.3%)	64 (4.2%)
2017	54 (1.8%)	460 (3.9%)	448 (4.9%)	688 (4.7%)	66 (3.7%)
2018	66 (2.2%)	459 (3.9%)	491 (4.8%)	798 (5.0%)	116 (5.4%)
2019	67 (2.1%)	488 (4.1%)	625 (5.4%)	907 (4.8%)	205 (7.7%)
2020	27 (1.2%)	559 (4.9%)	620 (5.7%)	1,371 (7.0%)	174 (5.5%)
2021	47 (1.9%)	513 (4.5%)	726 (6.0%)	1,284 (6.1%)	179 (4.7%)

Source: 2015-2020 provided using NSDUH Public Data Analysis System (PDAS) system analysis of Public Use File ([SAMHSA 2023](#)). 2021 estimates provided using custom SAMHSA analysis of Restricted Use File ([CBHSQ 2022a](#)).

Note: Analysis excluded under 1% of observations with values coded as "bad data" (i.e., usually inconsistent with other data). People who used marijuana in the past year but did not specify whether their use was recommended by a doctor or other healthcare professional were excluded (<1%).

Data cited at ([FDA Office of Surveillance and Epidemiology, 2023](#)), Appendix Tables 7.7.7 to 7.7.11.

Individuals without an HCP recommendation for marijuana use were more likely to report use of marijuana in the 30 days prior compared to those with HCP recommended use while the opposite pattern was observed in the 241-365 days prior ([Table 9](#)).

Table 9. Frequency of Marijuana Use in the Past Year, by Age Group: Among Past-Year Marijuana Users With Different Use Types Aged 12 or Older, NSDUH, 2021 (Numbers in Thousands)

Frequency	Weighted Frequency in Thousands	Weighted Prevalence (%)
All Past-Year Marijuana Users		
1-30 days	19,610	37.4
31-60 days	5,446	10.4
61-180 days	7,704	14.7
181-240 days	2,868	5.5
241-365 days	16,826	32.1

	Unweighted Response to Threatened Response Ratio	Weighted Response Ratio
Answer 1: Do you believe that the threat posed by terrorism is a threat to the United States?		
All U.S. respondents	17.2%	20.7
U.S. born respondents	15.7%	17.1
U.S. born, U.S. born parents	15.0%	16.4
U.S. born, U.S. born parents	15.0%	16.4
U.S. born, U.S. born parents	15.0%	16.4
Answer 2: Do you believe that the threat posed by terrorism is a threat to the United States?		
All U.S. respondents	6.0%	10.7
U.S. born respondents	5.7%	9.4
U.S. born, U.S. born parents	5.0%	10.3
U.S. born, U.S. born parents	5.0%	10.3
U.S. born, U.S. born parents	5.0%	10.3
Answer 3: Do you believe that the threat posed by terrorism is a threat to the United States?		
All U.S. respondents	1.0%	11.4
U.S. born respondents	1.0%	10.9
U.S. born, U.S. born parents	1.0%	10.0
U.S. born, U.S. born parents	1.0%	10.0
U.S. born, U.S. born parents	1.0%	10.0

Note: The weighted response ratio is calculated by multiplying the unweighted response ratio by the weight of the respondent. The weight of the respondent is calculated by dividing the number of respondents in the same category by the total number of respondents in the survey.

Source: The author's analysis of the data from the 2001 National Survey of the Attitudes of Americans Toward Terrorism. The survey was conducted by the Center for Strategic Studies, the University of Virginia, and the Center for the Study of Terrorism and the Unconquered, the University of Virginia.

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Table 10: Schedule of Operating and Maintenance Costs (Amounts in \$1000s) for the City of Seattle for the Fiscal Year 2025

Category	Operating and Maintenance Costs	Capital Costs	Total Costs
Police Department	1,200,000	50,000	1,250,000
Fire Department	800,000	30,000	830,000
Public Works Department	600,000	20,000	620,000
City Administration	400,000	10,000	410,000
Other Departments	200,000	5,000	205,000
Total	3,200,000	115,000	3,315,000

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4.1.2.3. Discussion

Nearly all adolescents who used marijuana in the year prior did not have an HCP recommendation. Overall, older individuals appeared to be more likely to have used marijuana only under an HCP recommendation than the younger age groups. The large majority of individuals who used marijuana in the past year as per HCP recommendation bought or paid for it, often from a dispensary.

Because SAMHSA restricted the question to use of marijuana as per HCP recommendation, the results reflect the proportion of respondents for which use of marijuana is supported by medical judgment. However, HCP's ability to provide such recommendation is likely influenced by the legal status of the state of residence.

The coronavirus disease of 2019 (COVID-19) pandemic disrupted NSDUH data collection in 2020 and 2021 ([FDA Office of Surveillance and Epidemiology, 2023](#)). Thus, the 2020 results reflect a combination of results collected in the first 3 months of 2020, prior to the beginning of COVID-19 restrictions, and the last 3 months of 2020, which consisted of a mix of in-person collection in areas where COVID-19 rates were low and web-based data collection in other areas. In 2021, SAMHSA collected data both in-person and online web-based surveys, and the frequency of collection mode varied by quarter, with more in-person surveys in later quarters than in earlier quarters. SAMHSA also found mode effects as in-person respondents were more likely to have used certain substances and more likely to have experienced mental health issues than online respondents ([FDA Office of Surveillance and Epidemiology, 2023](#)).

4.1.3. Behavioral Risk Factor Surveillance System (BRFSS)

4.1.3.1. Methods

BRFSS is a national state-based cross-sectional telephone survey that collects data on health-related risk behaviors, chronic health conditions, and use of preventive services from more than 400,000 noninstitutionalized adults ages 18+ years each year ([CDC 2018](#)). Initially established in 1984 in 15 states by the CDC, the survey is currently administered by state health departments—with technical and methodological assistance from CDC—in all 50 states, the District of Columbia, and three U.S. territories. The states use a standardized core questionnaire, optional modules (including a module on marijuana use),¹³ and state-added questions.

FDA analyzed BRFSS data for the calendar year 2021, which included a combination of core and marijuana module-specific questions from states and territories that participated in the optional marijuana questionnaire. Marijuana module data included questions on 1) past 30-day marijuana use, 2) reasons for using marijuana (i.e., medical, non-medical, or

¹³ The states and territories participating in the optional marijuana module are Alaska, Connecticut, Delaware, Guam, Hawaii, Idaho, Illinois, Indiana, Kentucky, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New York, North Dakota, Ohio, Oklahoma, Rhode Island, Utah, Vermont, and Wyoming.

both), and 3) method of use (i.e., smoking, eating, drinking, vaporizing, dabbing, or other). Response rates for BRFSS were calculated using standards set by the American Association for Public Opinion Research (AAPOR) Response Rate Formula. In 2021, the overall median survey response rate was 44.0% and ranged from 23.5 to 60.5% across all states/territories that participated. FDA reported population-level estimates based on complex survey weights and survey designs that adjusted for nonresponse bias and non-coverage areas. Additional details are described in the CDC's BRFSS website ([CDC 2023](#)).

4.1.3.2. Results

A total of 182,212 adults ages ≥18 years residing in the participating states and territories responded to the marijuana module in 2021, representing an estimated weighted frequency of 68,152,868 individuals. These individuals were mostly White, Non-Hispanic (67.0%, 95% CI: 66.5, 67.5), Black, Non-Hispanic (11.8%, 95% CI: 11.4, 12.2), or Hispanic (10.5, 95% CI: 10.1, 10.9). Their age distribution is shown in [Table 12](#).

Table 12. Distribution by Age Group of Respondents, BRFSS 2021

Age (Years)	Frequency	Weighted		
		Frequency	Percent	95% Confidence Limits
18-24	9,390	7,830,004	11.3	11.1 11.9
25-34	17,605	11,077,448	16.3	15.8 16.7
35-44	23,483	10,905,138	16.0	15.6 16.5
45-54	27,902	10,528,936	15.4	15.1 15.9
55-64	35,616	11,614,979	17.0	16.7 17.4
65+	68,216	16,196,364	23.8	23.4 24.2
Total	182,212	68,152,868	100.0	- -

Of them, a total of 17,889 individuals reported past 30-day use of marijuana, representing a weighted prevalence rate of 11.9% (95% CI: 11.5, 12.3). Among them, 56.9% (95% CI: 55.3, 58.6) were male, 66.6% (95% CI: 65.1, 68.1) White, Non-Hispanic, and 15.0% (95% CI: 13.6, 16.3) Black, Non-Hispanic. Their age distribution is shown in [Table 13](#).

Table 13. Distribution by Age Group of Respondents Who Reported Past 30-Day Marijuana Use, BRFSS, Marijuana Module, 2021

Age (Years)	Frequency	Weighted		
		Frequency	Percent	95% Confidence Limits
18-24	2,001	1,654,965	20.6	19.1 22.2
25-34	3,512	2,292,084	28.6	27.0 30.2
35-44	3,349	1,485,146	18.5	17.3 19.7
45-54	2,620	954,256	11.9	10.9 12.9
55-64	3,287	1,033,302	12.9	11.9 13.9
65+	2,897	507,458	7.5	6.8 8.1
Total	17,866	8,017,412	100.0	- -

* Excludes individuals who responded, "Don't know/not sure" and those who refused to answer.

A total of 24.9% (95% CI: 23.6, 26.2) reported use for medical reasons and 38.8% (95% CI: 37.2, 40.5) for both medical and nonmedical reasons ([Table 14](#)). Reason for use in the participating states or territories is shown in the Appendix (Appendix, [Table 63](#)).

Table 14. Past 30-Day Marijuana Use by Reason for Use, BRFSS, Marijuana Module, 2013
Percentages for Past 30 Days

Marijuana Use	Frequency	Percentage	Weighted %
Medical reasons	1,300	1,001.423	10.11443 (9.7)
Recreational use	1,000	1,010.509	10.11718 (9.7)
Total (both)			20.23161

Overall, past 30-day use of marijuana for medical reasons increased with age with 12.6% (95% CI: 10.1, 15.1) of individuals ages 18-24 years and 37.1% (95% CI: 31.1, 43.1) of individuals ages 65+ years reporting to use exclusively for this purpose ([Table 13](#)). Conversely, past 30-day use of marijuana for recreational reasons decreased with increasing age with 44.8% (95% CI: 44.3, 53.1) of individuals ages 18-24 years and 32.3% (95% CI: 28.4, 36.1) of individuals ages 65+ years. Among individuals who reported past 30-day use of marijuana for both medical and recreational reasons, although this overlap use appears to decrease starting from age 35 years with 30.6% (95% CI: 24.8, 36.3) of individuals ages 65+ years reporting to dual use.

Table 15. Past 30-Day Use of Marijuana by Age Category and Stratified by Reason of Use, BRFSS, Marijuana Module, 2021

Age Group (Years)	Any Reason		Nonmedical Reason		Medical Reason		Both Medical and Nonmedical Reason	
	Frequency	Weighted Frequency	Weighted Frequency (%)	Weighted % (95% CI)	Weighted Frequency (%)	Weighted % (95% CI)	Weighted Frequency (%)	Weighted % (95% CI)
18-24	2,001	1,654,965	807,187	48.8 (44.5, 53.1)	208,576	12.6 (10.1, 15.1)	639,203	38.6 (34.4, 42.8)
25-34	3,512	2,292,084	859,936	37.5 (34.2, 40.9)	444,111	19.4 (17.0, 21.7)	988,037	43.1 (39.8, 46.4)
35-44	3,349	1,485,146	491,771	33.1 (29.9, 36.3)	401,714	27.0 (24.1, 30.0)	591,662	39.8 (36.4, 43.3)
45-54	2,620	954,256	251,969	26.4 (22.8, 30.0)	336,105	35.2 (31.3, 39.2)	366,182	38.4 (33.9, 42.9)
55-64	3,287	1,033,502	301,838	29.2 (25.5, 32.9)	385,463	37.3 (33.2, 41.4)	346,201	33.5 (29.6, 37.4)
65+	2,897	597,458	192,731	32.3 (28.4, 36.1)	221,613	37.1 (33.1, 41.1)	183,114	30.6 (26.8, 34.5)
Total	17,666	8,017,412	2,905,432	36.2 (34.6, 37.8)	1,997,581	34.9 (23.6, 26.2)	3,114,399	38.8 (37.2, 40.5)

* Excludes individuals who responded, "Don't know/not sure" and those who refused to answer.

Regardless of the reason for use, data showed that smoking was the most frequent method of use with 60.3% (95% CI: 57.5, 63.1) among medical users and 73.9% (95% CI: 71.6, 76.3) among those who reported both medical and recreational use (Appendix, [Table 64](#)). Edibles represented 21.3% (95% CI, 19.1, 23.5) of method of use among medical users and 12.6% (95% CI: 10.7, 14.5) among those who reported both medical and recreational use.

4.1.3.3. Discussion

CDC's BRFSS survey data suggest that, among those who report past 30-day use of marijuana, medical use increases with increasing age. Regardless of the reason for use, smoking and edibles were the most frequent methods of use.

Besides limitations inherent to survey research, which include the cross-sectional nature of the data and potential for response bias, the BRFSS data were limited to the 24 states and territories that participated in the 2021 module on marijuana use. Also, response rates differed widely across states and territories with some states having survey response rates as low as 23.5%.

4.1.4. Monitoring the Future (MTF)

4.1.4.1. Methods

Since 1975, MTF collects information on medical and nonmedical use of selected prescription and illicit drugs and alcohol by conducting an annual, nationally representative, cross-sectional survey of 8th, 10th, and 12th graders ([NIDA 2022](#)). The survey is funded by the NIDA, a component of the National Institutes of Health (NIH), and conducted by the University of Michigan. Schools are invited to participate in the MTF study for a 2-year period ([Miech et al. 2023](#)). Informed consent (active or passive, per school policy) is obtained from parents of students younger than 18 years and from students aged 18 years or older. Starting in 2017, the survey included information on marijuana use under a doctor's recommendation.

To secure a nationally representative sample of high school seniors, the survey uses a three-stage sampling procedure, sampling geographic regions, schools, and individual students. MTF used paper-and-pencil surveys prior to 2019, and in 2019, a randomly selected half of students were administered paper-and-pencil surveys while the other half recorded their answers on electronic tablets. From 2020, all students recorded their responses using electronic tablets. In-school data collection stopped on March 15, 2020, as a result of the COVID-19 pandemic resulting in a sample size for the calendar year 2020 that was 25% of the size of a typical data collection.

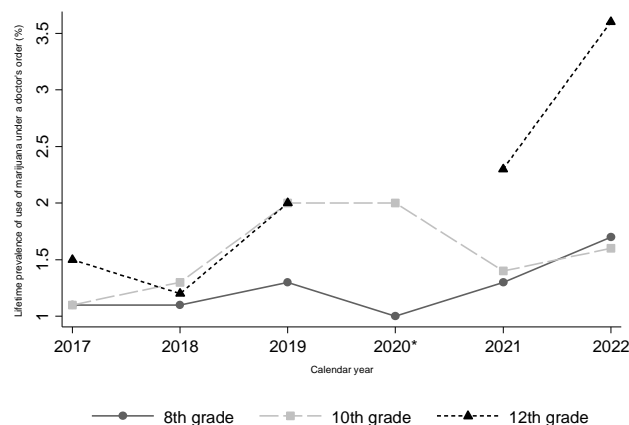
FDA abstracted data on response rate and lifetime prevalent use of marijuana under a doctor's recommendation from the National Survey Results on Drug Use, 1975-2022: Secondary School Students ([Miech et al. 2023](#)). Additional details are described elsewhere ([FDA Office of Surveillance and Epidemiology, 2023](#)).

4.1.4.2. Results

The survey included the lowest number of students in 2020 (n=11,821) and the highest in 2018 (n=44,482) with a response rate across the entire study period of $\geq 82\%$ among 8th graders, $\geq 78\%$ among 10th graders, and $\geq 69\%$ among 12th graders (Appendix [Table 65](#)).

The lifetime prevalent use of marijuana under a doctor's recommendation among 8th graders ranged from 1.1% in 2017 to 1.7% in 2022 ([Figure 1](#)). The lifetime prevalence among 10th graders ranged from 1.1% in 2017 to 1.6% in 2022, although peaking up to 2.0% in 2019 and 2020. The lifetime prevalence of use among 12th graders ranged from 1.5% in 2017 to 3.6% in 2022.

Figure 1. Prevalence of Use of Marijuana Under a Doctor's Order in Grades 8th, 10th, and 12th, MTF, 2017–2022



* Insufficient data for the 2020 estimate in 12th graders, due to curtailed data collection during the COVID-19 pandemic.

4.1.4.3. Discussion

NIDA's MTF data suggest that lifetime prevalent use of marijuana under HCP recommendation among 8–12th graders is rare ($<3.6\%$). Because this survey is school-based (and not household-based) it does not provide estimates of prevalence of use for dropouts and home-schooled teenagers.

4.1.5. Conclusions on Patterns of Medical Use

FDA examined patterns of use among medical users of marijuana as reported in four U.S. national surveys: ICPS, SAMHSA's NSDUH, CDC's BRFSS, and NIDA's MTF. In

general, most data sources other than ICPS lacked details on patient characteristics and factors that promoted the use of marijuana for medical purposes. Some data sources were impacted by the COVID-19 pandemic, and, for ICPS and BFRSS data were largely restricted to the calendar year 2021. Despite these limitations, these data suggest that medical use increases as age increases. NSDUH data suggested that individuals who reported use as per an HCP recommendation were more likely to use marijuana more frequently over the year compared to those without any recommended use. Only data from ICPS provided information on intended indication for use, which suggested that medical users often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms. In ICPS, approximately 50-60% of exclusive medical users reported having ever asked an HCP for a recommendation to use medical cannabis. In 2021, as per BRFSS data, smoking appears to be the most frequent method of use and, as per ICPS, at least 40% of individuals reported using cannabis and alcohol simultaneously. Generally, medical users reported obtaining cannabis through different sources with stores and dispensaries being the most commonly reported cannabis source, followed by family and friends.

4.2. University of Florida Systematic Literature Review

The purpose of Section [II.4.2](#) is to summarize the findings from a systematic literature review of the credible evidence of effectiveness and safety of marijuana as a medical treatment for the indications of anorexia, anxiety, epilepsy, inflammatory bowel disease (IBD), nausea, pain, and post-traumatic stress disorder (PTSD).

4.2.1. Methods

The University of Florida (UF), under contract with FDA, conducted a series of systematic reviews to critically evaluate and interpret literature on patient-level controlled observational and controlled interventional studies (original research or systematic reviews/meta-analyses of original research) evaluating the effectiveness of marijuana for the treatment of anorexia³, anxiety, epilepsy, inflammatory bowel disease, nausea,¹⁴ pain, and PTSD. They also evaluated the potential harms from marijuana use as they relate to these seven indications.

The seven indications that were identified for further analysis were determined by FDA, in part informed by OASH's findings under Part 1 of the CAMU test and in part informed by FDA's own analysis of the landscape in which marijuana is currently used medically, including information from state-level programs on how and to what extent marijuana is being utilized for medical purposes. The FDA analysis of the landscape was to determine the most appropriate indications to be further evaluated, including by the UF team in a systematic literature review. The landscape analysis was based on the following: a representative sample of available state-level data on authorized medical uses, expedited review of key professional organizations' recommendations, indications for active

¹⁴ Broadly defined as inclusive of vomiting/emesis.

investigational new drug (IND) applications for all cannabinoids, preliminary PubMed search for topics related to marijuana, and currently FDA-approved cannabinoid product indications. Based on these factors considered, the chosen indications were based on state-level utilization, scientific interest (e.g., publications, INDs, professional organizations), and indications previously approved for other cannabinoids.

UF conducted searches, one per indication, in PubMed, the Cochrane Library, American Psychiatric Association (APA) PsycInfo, and Embase in February 2023. The search criteria, agreed upon with FDA, were defined according to marijuana exposure¹⁵ and indication-specific keywords and controlled vocabulary.¹⁶ The searches were restricted to publications in English and to the period between January 2000 through February 2023 to identify literature published since the 1999 Institute of Medicine's *Marijuana and Medicine* review ([IOM 1999](#)).

After removal of duplicates, screening, and assessment for eligibility by two independent reviewers (a third one in case of disagreement), all included studies were critically evaluated for risk of bias using the Cochrane risk-of-bias tool for randomized trials (RoB 2) or the "Risk of Bias In Non-randomised Studies - of Interventions" (ROBINS-I) ([Sterne et al. 2016](#); [Sterne et al. 2019](#)). The RoB 2 contains assessment of risk of bias for five domains: 1) bias arising from the randomization process, 2) bias due to deviations from intended intervention, 3) bias due to missing outcome data, 4) bias in measurement of the outcome, and 5) bias in selection of the reported result. Within each of the five domains, raters respond to a series of questions that generate a numerical score per response. Based on the score total from each domain, the risk of bias within each of the domains is then ranked as "low risk", "some concern", or "high risk" as per pre-specified score thresholds. The ROBINS-I scores each study on seven domains: 1) bias due to confounding, 2) selection bias, 3) bias in classification of interventions, 4) bias due to deviations from intended interventions or measured exposure, 5) bias due to missing data, 6) bias in the measurement of outcomes, and 7) bias in the selection of reported results. Within each of the seven domains, raters respond to a series of questions that generate a numerical score per response. Based on the score total from each domain, the risk of bias within each of the domain is then ranked as "low", "moderate", "serious", or "critical". Each study was independently rated by two investigators; when there was disagreement amongst raters, a third investigator conducted an independent rating.¹⁷

Observational studies with serious or critical risk of bias and, for the pain indication, randomized controlled trials (RCTs) and observational studies that investigated the pain

¹⁵ The exposure definition excluded FDA-approved cannabis-derived products, hemp as defined in the 2018 Farm Bill, topical formulations, synthetic forms of Δ^9 -THC, and combinations of marijuana and synthetics except in cases where the effects of an exposure for the marijuana agent were investigated separately from the combination.

¹⁶ Controlled vocabulary represents the standardized words and phrases employed by databases to organize literature on related subjects.

¹⁷ As specified in the protocol, studies where two out of three raters did not achieve consensus, quality rating was determined by a faculty team lead.

as a secondary outcome, were not further considered. For the remaining RCTs and observational studies, evidence quality was rated for primary outcome(s) assessed within each indication (rather than for individual studies) in accordance to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach within the Cochrane handbook ([Schünemann et al. 2019](#)).¹⁸ The rating for each outcome was informed by the rating assessment of five quality domains (Certainty, Imprecision, Inconsistency, Generalizability, and Publication Bias). The GRADE approach allows raters to promote or demote 'Certainty' in the evidence rating based on several criteria. To demote 'Certainty' in evidence, key considerations included risk of bias, imprecision, inconsistency, indirectness, and publication bias.¹⁹ To promote 'Certainty' in evidence, key considerations included large magnitude of effect, dose-response gradient, and residual confounding that would decrease the magnitude of effect (where an effect was observed or reported). In cases where an outcome was only assessed in a single study, the raters were unable to rate the domain of 'Inconsistency' as this describes consistency in direction of findings as compared across studies (or across analysis groupings if multiple analyses of the outcome are reported within a single study). The overall quality of evidence rating was stated as a categorical judgement ([Table 16](#)).

Table 16. Categories and Definitions for the Overall Evidence Quality Ratings*

Evidence Quality Rating	Definition of Rating
Very low quality	The true effect of marijuana is probably significantly different from the estimated (reported or observed) effect.
Low quality	The true effect of marijuana may be similar to the estimated (reported or observed) effect.
Moderate quality	The true effect of marijuana is probably similar to the estimated (reported or observed) effect.
High quality	The true effect of marijuana is similar to the estimated (reported or observed) effect.

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

* Based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach

Quantitative meta-analysis, including pooled estimates and/or meta-regressions as applicable, were calculated in instances where a minimum of five studies reported the outcome with sufficient homogeneity in reporting to support a pooled estimate. Additionally, FDA required that the studies reporting that outcome be rated as 'moderate' or 'high' quality evidence to avoid amplifying bias in reported effects that may be present in lower quality studies.

For a full list of references that were considered for the systematic literature review, refer to the Appendix under each listed indication (Sections [III.5.1](#), [III.5.2](#), [III.5.3](#), [III.5.4](#), [III.5.5](#), and [III.5.6](#)). All the information included in this section is based on the UF review; the Appendix provides the references for the RCTs, observational studies, and supporting literature relevant to the text included in this review ([Table 81](#), [Table 83](#), [Table 85](#), [Table 87](#), [Table 89](#), [Table 91](#)).

¹⁸ The RCTs with 'high' risk of bias were considered in quality of evidence ratings, but resulted in evidence quality rating demotion as per Cochrane guidance.

¹⁹ The risk of bias assessments conducted prior to the evidence rating activity informed these decisions.

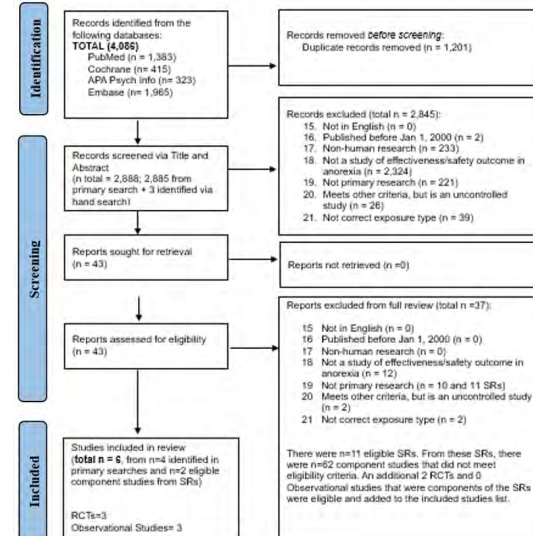
Further methodological details, including these in data extraction, screening, assessment of eligibility, risk of bias, assessment of quality of evidence, synthesis, and presentation of the data, are described in the Cochrane Review for Molecular Epidemiology of Chemical Carcinogens (2009) (10).

4.3.3.2. Studies

Abstracts and/or full-text articles were screened in many field conditions, such as cancer and infectious diseases, using PubMed (11). The abstracts that the largest panel of reviewers (12) found relevant were included. In particular, epidemiological studies (2005), such as genetic epidemiology studies (2006), were included. The abstracts that were not included in the abstracts were screened in a complete process, particularly regarding epidemiological studies. Finally, screening was a generalized criterion for selection.

The abstracts of the studies of the scientific literature published after a 2004 publication, after removal of duplicates, screening, and assessment for eligibility, those studies that met the eligibility criteria, those of the studies already identified in the literature, and those that were selected from the Cochrane Review for Molecular Epidemiology of Chemical Carcinogens (2009) (10) were included in the synthesis of epidemiological studies (2006). When the data studies were not available, the abstracts of the studies were included. When the data studies were not available, the abstracts of the studies were included. When the data studies were not available, the abstracts of the studies were included.

Figure 2. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Anorexia



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023

The three observational studies eligible for inclusion were not considered further because each was rated as having a critical risk of bias. Thus, only three RCTs were further considered; each one of them examined different sets of outcomes among the following: (1) appetite, (2) quality of life, (3) food intake, and (4) body weight. The quality of evidence rating for the studies by outcome are shown in [Table 17](#), [Table 18](#), [Table 19](#), [Table 20](#). There were insufficient studies of moderate or high quality to support the calculation of meta-analytic estimates for any of the outcomes within the anorexia indication.

Table 17. Quality of Evidence Rating for Appetite, Certainty Rating by Study and Overall

Domain Assessed	(Strasser et al. 2006)	Overall Certainty Rating Across Studies
Certainty	High concern	High concern
Imprecision	High concern	High concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Unable to rate
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 18. Quality of Evidence Rating for Quality of Life, Certainty Rating by Study and Overall

Domain Assessed	(Strasser et al. 2006)	Overall Certainty Rating Across Studies
Certainty	High concern	High concern
Imprecision	High concern	High concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Unable to rate
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 19. Quality of Evidence Rating for Food/Caloric Intake, Certainty Rating by Study and Overall

Domain Assessed	(Hanev et al. 2005)	(Hanev et al. 2007)	Overall Certainty Rating Across Studies
Certainty	Moderate concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Moderate concern	Moderate concern
Inconsistency			Low concern
Generalizability	Moderate concern	Moderate concern	Moderate concern
Publication bias			Unable to rate
Overall quality of evidence rating			Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 20. Quality of Evidence Rating for Body Weight, Certainty Rating by Study and Overall

Domain Assessed	(Hanev et al. 2007)	Overall Certainty Rating Across Studies
Certainty	Moderate concern	Moderate concern
Imprecision	Unable to rate	Unable to rate
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Unable to rate
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Summary of Effectiveness for Anorexia

The studies assessed the benefit of therapeutic algorithms on several outcome measures related to BVD anorexia outcomes. In participants with BVD, there was moderate quality of evidence that patients increased caloric intake and the quality of evidence that patients increased body weight. One of these studies showed a significant increase in weight in participants but only in those participants who had significant loss of muscle mass prior to treatment. The other study showed an increase in caloric intake in participants with BVD. One RCT showed patients had any benefit in cancer-related quality and showed no benefit compared with placebo. There was no significant effect of treatment on the occurrence of impaired appetite or quality of life, in any of the RCTs based on a low quality of evidence.

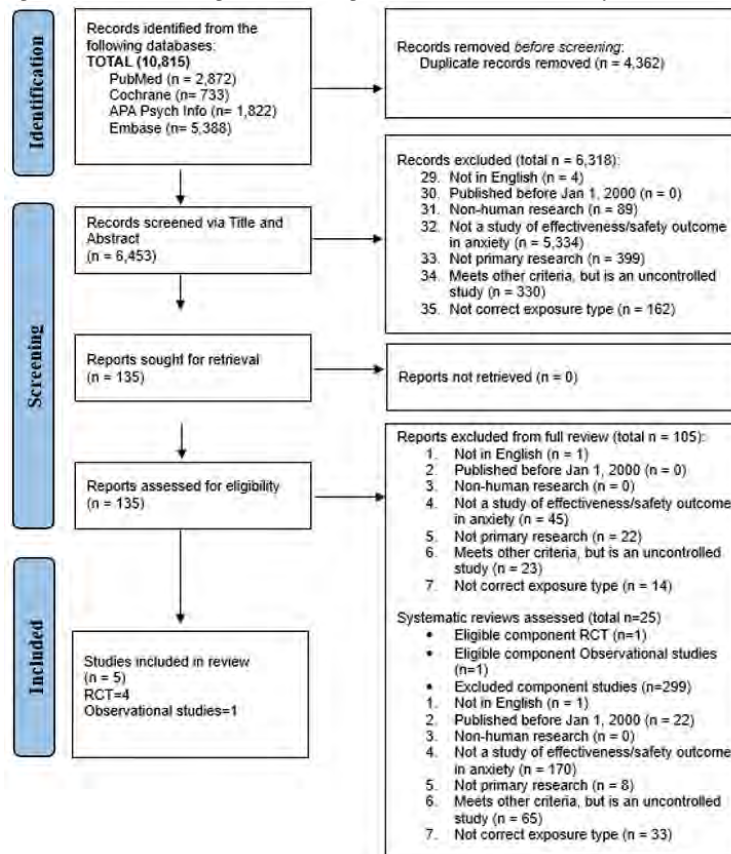
Summary of Safety for Anorexia

A higher proportion of patients experienced adverse events (AEs) with treatment compared to placebo in one study but not in the others examined by USP. No serious adverse events (SAEs) were reported in these studies.

4.2.2.2. Anorexia

The study population is characterized broadly throughout the text and includes other neuromuscular diseases such as guinea pig myopathy and (GABA), depression, and depression. Therefore, some have hypothesized that anorexia may impact quality and safety-related outcomes through its effects on the neuromuscular system. The connection to the scientific literature indicated a need for clinical guidelines. After review of all guidelines, screening, and assessment for eligibility, USP identified five studies relevant to the indication of anorexia where patients are affected by several conditions with anorexia-related outcomes. These included: bulimic, obsessive-compulsive disorder (OCD), multiple sclerosis, Parkinson disease, and non-specific pain. Nine of the identified studies included a primary anorexia disorder. Four were RCTs and five were observational studies ([Figure 2](#)). The summary of studies included in the risk of bias assessment is available in the document and full of this assessment is displayed in Appendix [Table 2](#).

Figure 3. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Anxiety



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

The observational study was rated with sufficiently low risk of bias to be included in quality of evidence ratings along with the four RCTs, all of them categorized as having low risk of bias. Each one of the studies assessed examined different sets of outcomes among the following: (1) Self-Rating Anxiety Scale; Symptom Checklist-90 (SCL-90); Spielberger State-Trait Anxiety (STAI-S); (2) Profile of Mood States; (3) Fibromyalgia Impact Questionnaire- Anxiety Component; and (4) HADs- Quality of Life Component. The quality of evidence rating for the studies by outcome are shown in [Table 21](#).

[Table 22](#), [Table 23](#), [Table 24](#). The studies did not report sufficiently homogeneous outcomes to be eligible for meta-analysis calculations per outcome.

Table 21. Quality of Evidence Rating for Anxiety Scales (Self-Rating Anxiety Scale; Symptom Checklist-90; Spielberger State-Trait Anxiety), Certainty Rating by Study and Overall

Domain Assessed	(Aragona et al. 2009)	(Kavser et al. 2020)	Overall Certainty Rating Across Studies
Certainty	Low concern	Low concern	Low concern
Imprecision	Moderate concern	Low concern	Moderate concern
Inconsistency			Moderate concern
Generalizability	High concern	High concern	High concern
Publication bias			Low concern
Overall quality of evidence rating			Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 22. Quality of Evidence Rating for Profile of Mood States, Certainty Rating by Study and Overall

Domain Assessed	(Ware et al. 2015)	Overall Certainty Rating Across Studies
Certainty	Moderate concern	Moderate concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to Rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Low concern
Overall quality of evidence rating		Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 23. Quality of Evidence Rating for Fibromyalgia Impact Questionnaire: Anxiety Component, Certainty Rating by Study and Overall

Domain Assessed	(Chaves et al. 2020)	Overall Certainty Rating Across Studies
Certainty	Low concern	Low concern
Imprecision	Low concern	Low concern
Inconsistency		Unable to Rate
Generalizability	High concern	High concern
Publication bias		Low concern
Overall quality of evidence rating		Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 24. Quality of Evidence Rating for HADs: Quality of Life Component, Certainty Rating by Study and Overall

Domain Assessed	(Kanjanaarangsichai et al. 2022)	Overall Certainty Rating Across Studies
Certainty	Low concern	Low concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to Rate
Generalizability	High concern	High concern
Publication bias		Low concern
Overall quality of evidence rating		Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023

Summary of Effectiveness for Anxiety

None of the RCTs showed any improvement in anxiety outcome measures and potentially worsened symptoms of paranoia or performed worse than placebo (in obsessive compulsive disorder) based on a moderate quality of evidence. THC-rich cannabis oil showed a significant decrease in symptoms of fibromyalgia and improvement in quality of life based on the Fibromyalgia Impact Questionnaire (FIQ) score compared to the placebo group and baseline scores. However, this questionnaire and findings are not specific to anxiety.

The observational study was a prospective cohort study with the primary objective of assessing the safety of cannabis use as a self-management strategy for chronic non-cancer pain. Secondary efficacy parameters included mood, which was measured using the Profile of Mood States. This study reported that individuals who used cannabis experienced significant improvement in total mood disturbance scale compared to controls, with improvements observed in the tension-anxiety, depression-dejection, anger-hostility, and fatigue-inertia subscales. Despite low concerns in other domains, this outcome was assessed by the UF investigators as having a moderate quality of evidence rating as it was driven by a moderate risk of bias in the reporting of the study outcome (investigators who assessed the outcomes were not blinded to cannabis treatment status) together with a moderate concern regarding imprecision in the reported effect.

Summary of Safety for Anxiety

The studies reported varying levels of adverse events with no increased risk of SAEs reported relative to the control group in the controlled studies. Marijuana was associated with an increased risk of AEs related to nervous system disorders, psychiatric disorders, and respiratory events when compared to placebo. A study conducted in multiple sclerosis patients treated with marijuana plant extract did not induce psychopathology or impair cognition in marijuana-naïve patients, but a positive correlation was found between blood levels of THC and psychopathological scores.

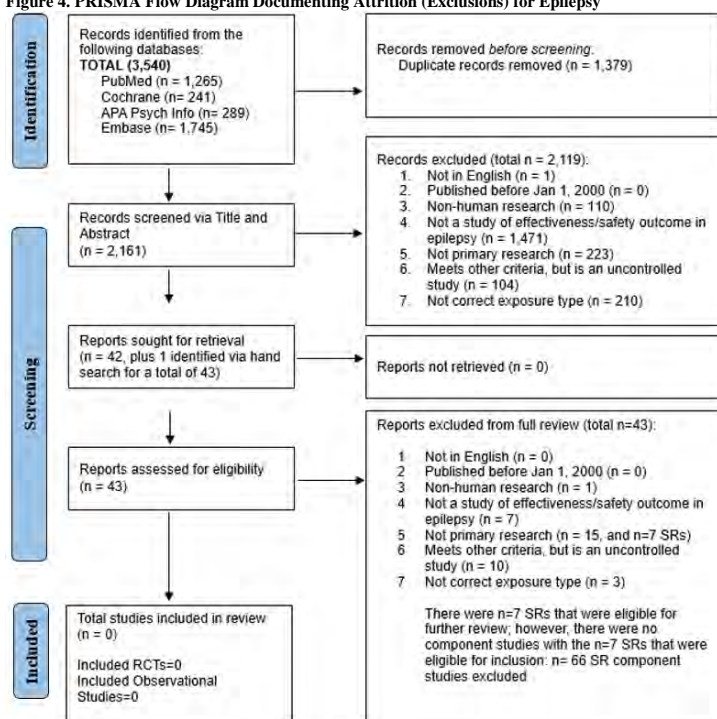
4.2.2.3. Epilepsy

The first FDA-approved cannabis-derived cannabidiol (CBD) human drug product (Epidiolex, GW Research, Ltd., Research Triangle Park, NC, approved in June 2018) is currently indicated for the treatment of seizures associated with Lennox-Gastaut

syndrome, Dravet syndrome, or tuberous sclerosis complex in patients 1 year of age or older ([Greenwich Biosciences 2018](#)). The precise mechanisms by which Epidiolex exerts its anticonvulsant effect in humans are unknown. CBD does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors ([Greenwich Biosciences 2018](#)). While CBD has clearly shown anti-seizure properties, contradictory pro-convulsant and anti-seizure effects have been reported for delta-9-tetrahydrocannabinol (Δ^9 -THC) ([Li et al. 2023](#)).

The searches identified a total of 3,540 studies. After removal of duplicates, screening, and assessment for eligibility, there were no studies (nor component studies included in the systematic reviews) that met all the protocol-specified criteria for inclusion in the review for the indication of epilepsy ([Figure 4](#)).

Figure 4. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Epilepsy



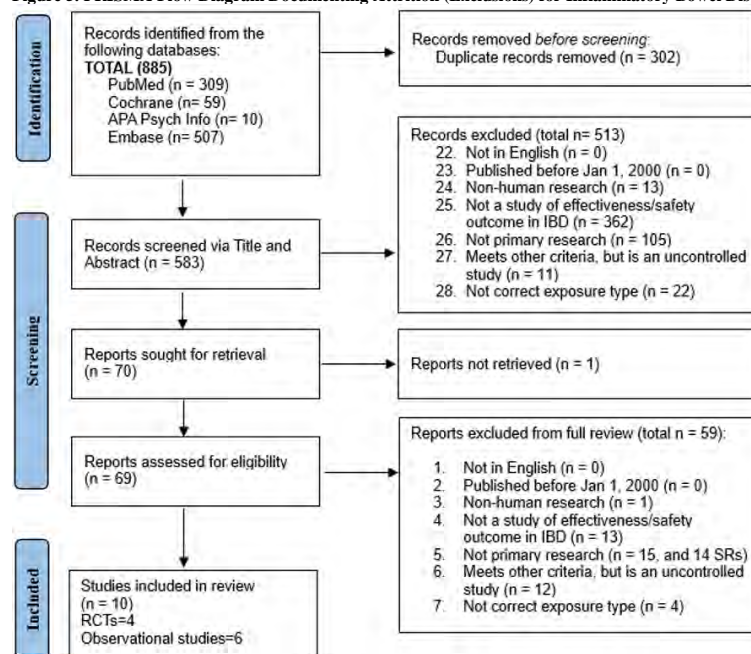
Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

4.2.2.4. Inflammatory Bowel Disease

The endocannabinoid system (ECS) plays a key role in regulating several gastrointestinal functions and is also involved in immune function, suggesting that it may be a viable target for treating inflammatory bowel disease (IBD).

UF's searches identified 885 records. After removal of the duplicated records and article screening, 10 records were included in the review (four RCTs and six observational studies) (Figure 5). Numerous outcomes were utilized in these studies, and not all studies identified a primary endpoint and/or adjusted for multiplicity. Most of the studies included patients with mild to moderate disease severity. Summary of studies included in the risk of bias assessments as well as their references and risk of bias assessment are displayed in Appendix III.5.3.

Figure 5. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Inflammatory Bowel Disease



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/IB Report dated July 19, 2023.

The six observational studies eligible for inclusion were not considered further because each was rated as having a serious or critical risk of bias. The four RCTs assessed a total of 13 effectiveness outcomes: (1) Disease activity; (2) Quality of life; (3) Daily function,

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Table 25. Quality of Evidence Rating for Clinical Disease Activity Indexes (CDAI/Lichtiger/Mayo Score), Certainty Rating by Study and Overall

Domain Assessed	(Nafali et al. 2013)	(Nafali et al. 2021a)	(Nafali et al. 2021b)	(Irvine et al. 2018)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern	Moderate Concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Low concern	Low Concern	High concern	Moderate concern
Inconsistency					Moderate concern
Generalizability	Moderate concern	Moderate concern	Moderate concern	High concern	Moderate concern
Publication bias					Moderate concern
Overall quality of evidence rating					Moderate quality

Source: Consortium For Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 26. Quality of Evidence Rating for Daily Function, General Well-Being, General Effect on Health, Certainty Rating by Study and Overall

Domain Assessed	(Nafali et al. 2021a)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	High concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern
Overall quality of evidence rating		Low quality

Source: Consortium For Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 27. Quality of Evidence Rating for Quality of Life, Certainty Rating by Study and Overall

Domain Assessed	(Nafali et al. 2013)	(Nafali et al. 2021a)	(Nafali et al. 2021b)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Imprecision	Low concern	Low concern	Low concern	Low concern
Inconsistency				Moderate concern
Generalizability	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Publication bias				Moderate concern
Overall quality of evidence rating				Moderate quality

Source: Consortium For Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 28. Quality of Evidence Rating for Pain, Certainty Rating by Study and Overall

Domain Assessed	(Nahali et al. 2021a)	(Nahali et al. 2021b)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Low concern	Moderate concern
Inconsistency			Moderate concern
Generalizability	Moderate concern	Moderate concern	Moderate concern
Publication bias			Moderate concern
Overall quality of evidence rating	Moderate quality		

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2-1B Report dated July 19, 2023.

Table 29. Quality of Evidence Rating for Remission, Certainty Rating by Study and Overall

Domain Assessed	(Nahali et al. 2019)	(Nahali et al. 2021a)	(Lecina et al. 2019)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	High concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Inconsistency				Low concern
Generalizability	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Publication bias				Low concern
Overall quality of evidence rating	Moderate quality			

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2-1B Report dated July 19, 2023.

Table 30. Quality of Evidence Rating for Number of Bowel Movements/Stool Frequency, Certainty Rating by Study and Overall

Domain Assessed	(Nahali et al. 2021a)	(Nahali et al. 2021b)	(Julius et al. 2018)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Serious concern	Serious concern	Serious concern	Serious concern
Imprecision	Moderate concern	Low concern	Unable to report	Moderate concern
Inconsistency				Moderate concern
Generalizability	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Publication bias				Moderate concern
Overall quality of evidence rating	Low quality			

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Marijuana Use. Project 2-1B Report dated July 19, 2023.

Table 31. Quality of Evidence Rating for Rectal Bleeding, Certainty Rating by Study and Overall

Domain Assessed	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Serious concern
Imprecision	Serious concern
Inconsistency	Unable to rate
Generalizability	Moderate concern
Publication bias	Low concern
Overall quality of evidence rating	Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2:1B Report dated July 19, 2023.

Table 32. Quality of Evidence Rating for Weight, Certainty Rating by Study and Overall

Domain Assessed	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Low concern
Imprecision	Low concern
Inconsistency	Unable to rate
Generalizability	Moderate concern
Publication bias	Low concern
Overall quality of evidence rating	High quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2:1B Report dated July 19, 2023.

Table 33. Quality of Evidence Rating for Disease-Specific Quality of Life, Certainty Rating by Study and Overall

Domain Assessed	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern
Imprecision	Moderate concern
Inconsistency	Unable to rate
Generalizability	Moderate concern
Publication bias	Low concern
Overall quality of evidence rating	Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2:1B Report dated July 19, 2023.

Table 34. Quality of Evidence Rating for Bloating, Certainty Rating by Study and Overall

Domain Assessed	(Nafali et al. 2021a)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	High concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 35. Quality of Evidence Rating for Nausea, Certainty Rating by Study and Overall

Domain Assessed	(Nafali et al. 2021a)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Serious concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 36. Quality of Evidence Rating for Appetite, Certainty Rating by Study and Overall

Domain assessed	(Nafali et al. 2021a)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	High concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 37. Quality of Evidence Rating for Endoscopic Assessment (Simple Endoscopic Score; Mays Endoscopic Score); Certainty Rating by Study and Overall

Domain Assessed	Ostapenko et al. 2021a	Ostapenko et al. 2021b	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concerns	Moderate concerns	Moderate concerns
Imprecision	Moderate concerns	Moderate concerns	Moderate concerns
Inconsistency			Low concerns
Generalizability	Moderate concerns	Moderate concerns	Moderate concerns
Publishability bias			Moderate concerns
Overall quality of evidence rating			Moderate concerns

Source: Cochraine for Medical Marijuana Clinical Outcomes Research in Partnership with the National Institutes of Medical Literature and Data on Marijuana Use. Project 2 ER Report dated July 15, 2023.

Summary of Effectiveness for IBD

Four RCTs, each assessing one or more of 13 effectiveness outcomes, were included in the synthesis of evidence. Overall, within the four RCTs, marijuana demonstrated positive effects on the Lichtiger score (eight components of colitis disease activity), response rate, Subject Global Impression of Change (SGIC), self-reported mood, sleep, pain, bloating, appetite, general well-being, and satisfaction.

All four RCTs considered clinical disease activity [e.g., Lichtiger score, Crohn's disease activity index (CDAI), Mayo score], with heterogeneous results based on a moderate quality of evidence. Similarly, mixed results were shown for the Inflammatory Bowel Disease Questionnaire (IBDQ) score, which showed significant improvement in one study, but not in another. Additionally, two studies suggested an enhancement in the quality of life via the 36-Item Short Form Survey (SF-36), while one study contradicted this finding, with the overall evidence quality being rated as moderate. A similar level of evidence quality was observed for the impact on pain, although one study indicated no significant alteration in abdominal pain, all based on a moderate quality of evidence. The outcomes concerning remission (definitions and measures differed amongst studies), disease-specific quality of life, and endoscopic evaluations were also classified as having moderate evidence quality, with all studies indicating no significant alteration.

Several effectiveness outcomes were classified as having low evidence quality. Among these, nausea and rectal bleeding did not demonstrate a significant alteration in the included studies following treatment with cannabis. Daily function, general well-being, overall health impact, and bowel movement/stool frequency exhibited heterogeneous results, with the overall evidence quality being low. Lastly, bloating and appetite were also classified as having low evidence quality, with both outcomes showing improvement in the included studies.

Summary of Safety for IBD

The RCTs assessed adverse events, however, limited safety information was reported overall.

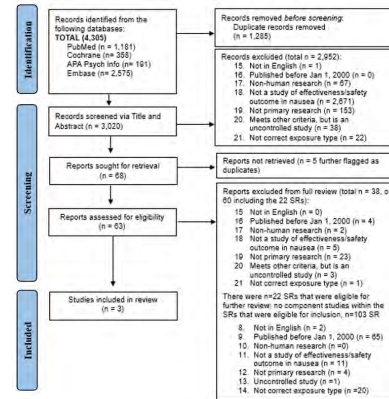
4.2.2.5. Nausea

Nausea and vomiting are common side effects of chemotherapy and in the postoperative setting, and currently there are two synthetic cannabinoids, dronabinol and nabilone, approved for treatment of chemotherapy-induced nausea and vomiting. Given established efficacy in clinical trials for the approved products and an established pharmacological pathway within the endocannabinoid system, marijuana has been studied to see if it exerts similar effects.

The literature searches identified a total of 4,305 studies. After removal of duplicates, screening, and assessment for eligibility, there were three studies, all RCTs, that met all the eligibility criteria. The risk of bias assessment suggested some concerns in one study and low risk of bias in two studies. The preferred reporting items for systematic reviews and meta-analysis (PRISMA) Flow Diagram Documenting Attrition (Exclusions) is

presented in [Figure 6](#). Summary of studies included in the risk of bias assessments as well as their references and risk of bias assessment are displayed in [Appendix III.5.4](#).

Figure 6. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Nausea



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Scientific Initiative: Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Each of the three RCTs reported one or more of three major outcome constructs, which were reported using one or more of 36 different metrics across the studies. They were grouped as follows (1) chemotherapy-induced nausea and vomiting; (2) nausea-specific quality of life (Functional Living Index-Emesis); general health-related quality of life; and (4) post-operative nausea and vomiting. The quality of evidence rating for the studies by outcome are shown in [Table 38](#), [Table 39](#), [Table 40](#), [Table 41](#).

Table 38. Quality of Evidence Rating for Chemotherapy-Induced Nausea and Vomiting, Certainty Rating by Study and Overall

Domain Assessed	(Grimsion et al. 2020)	(Duran et al. 2010)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Low concern	Low concern	Low concern
Imprecision	Moderate concern	High concern	Moderate concern
Inconsistency			Low concern
Generalizability	Moderate concern	Moderate concern	Moderate concern
Publication bias			Low concern

Overall quality of evidence rating:

Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 39. Quality of Evidence Rating for Nausea-Specific Quality of Life (Functional Living Index-Emesis (FLIE)), Certainty Rating by Study and Overall

Domain Assessed	(Grimsion et al. 2020)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Low concern	Moderate concern*
Imprecision	Low concern	Low concern
Inconsistency		Unable to rate
Generalizability	High concern	High concern
Publication bias		Moderate concern

Overall quality of evidence rating:

Low quality

*Certainty and generalizability ratings for nausea-specific quality of life relies on a single study with n=16 and another study indicating no improvement without sharing quantitative estimates (hence, not shown in this table).

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 40. Quality of Evidence Rating for Overall Health-Related Quality of Life, Certainty Rating by Study and Overall

Domain Assessed	(Grimsion et al. 2020)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	High concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern

Overall quality of evidence rating:

Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/18 Report dated July 19, 2023.

Table 41. Quality of Evidence Rating for Post-Operative Nausea and Vomiting, Certainty Rating by Study and Overall

Domain Assessed	(Kleine-Brueggene et al. 2015)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	High concern	High concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	Moderate concern	Moderate concern
Publication bias		Moderate concern
Overall quality of evidence rating		Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Per protocol, the RCTs did not meet thresholds for the minimum number of studies to qualify for any meta-analysis calculation.

Summary of Effectiveness for Nausea

Three RCTs were included in the analysis, and numerous outcome measures were assessed. Two of the three studies, which administered either THC-CBD extract or whole plant cannabis, showed benefit of marijuana compared with placebo. The quality of evidence rating of these studies was rated as moderate. The two positive studies assessed chemotherapy-induced nausea and vomiting in patients with refractory nausea after standard treatment, whereas the failed study assessed the effect of intravenous THC in the prevention of post-operative nausea and vomiting. Although the primary endpoint showed significant difference in two studies, it was noted that the effect was small and imprecise. Additionally, there was inconclusive or marginal benefit in the domains of quality of life, nausea-specific quality of life and post-operative nausea and vomiting, all based on a low quality of evidence. Overall, there is evidence supporting a positive effect of cannabis on chemotherapy-induced nausea and vomiting based on a moderate quality of evidence.

Summary of Safety for Nausea

A total of 98 patients were exposed to marijuana products in the three RCTs evaluated. A higher proportion were noted to experience AEs than placebo, but no excess risk of SAEs was reported. Adverse events reported were consistent with safety findings in other indications (e.g., sedation, dizziness, disorientation, dry mouth, anxiety). Although AEs were reported for marijuana, one study did show 83% of participants preferred marijuana to placebo.

4.2.2.6. Pain

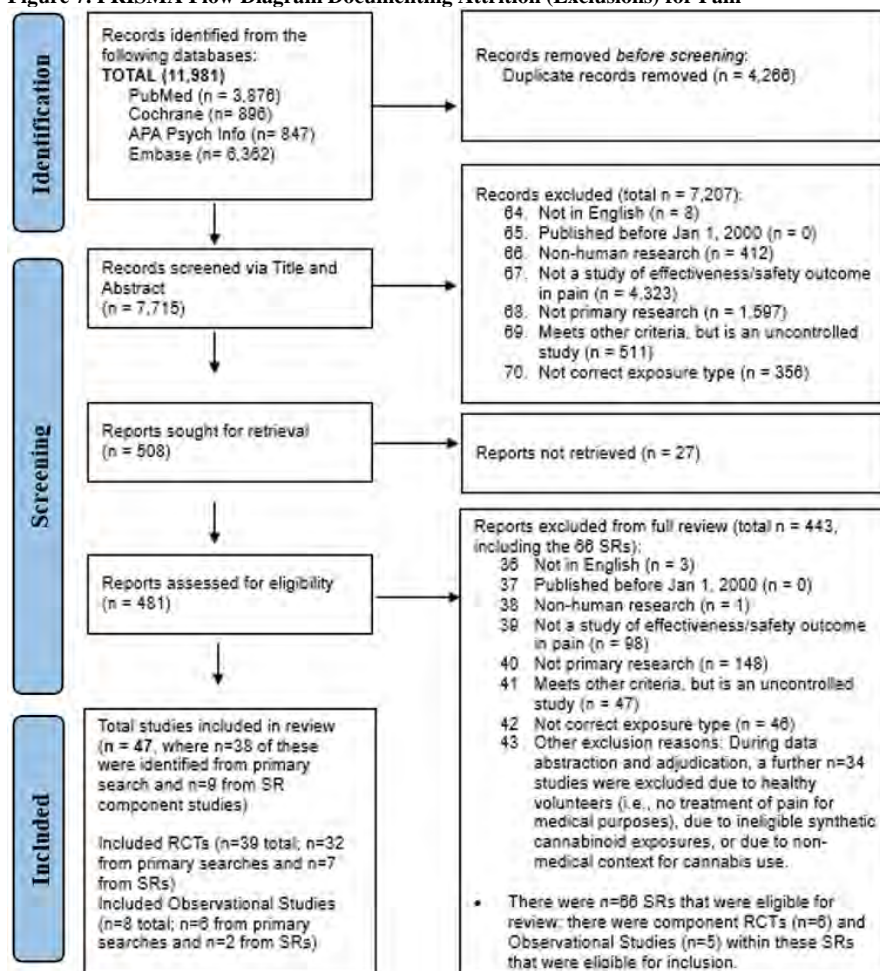
The UF reported noted that phytocannabinoids, including Δ^9 -THC, have been demonstrated by preclinical research to have analgesic effects in numerous types of pain (e.g., inflammatory or nociceptive pain, as well as neuropathic pain) according to a recent systematic review and meta-analysis of studies employing animal models. UF further noted that, in clinical research, a systematic review and meta-analysis concluded that marijuana products containing high THC-to-CBD ratios may be associated with short-

term improvements in chronic pain from neuropathic or non-cancer nociceptive pain sources.⁷ The UF review systematically examined evidence quality from studies that investigated effectiveness and safety of marijuana for the pain indication regardless of pain type (e.g., neuropathic, nociceptive, or cancer).

Pain has the most investigations amongst any of the indications in the review. The searches identified a total of 11,981 studies. After removal of duplicates, screening, and assessment for eligibility, there were 38 studies—32 RCTs and 6 observational studies—identified from the primary searches. Additionally, seven RCTs and two observational studies were identified from the eligible systematic reviews. Therefore, there were a total of 47 studies, 39 RCTs and 8 observational studies²⁰ that met all the protocol-specified criteria for inclusion in the review for the indication of pain (Figure 7). The summary of studies included in the risk of bias assessments, their references, and their risk of bias assessment are displayed in Appendix III.5.5.

²⁰ Two of the eight observational studies were included in other indications (i.e., anorexia and anxiety) as pain was a secondary outcome.

Figure 7. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Pain



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Seven of the eight eligible observational studies were not considered further as they were classified as having a serious or critical risk of bias assessment. The eighth observational study included pain as a secondary outcome; as described in the methods (Section [II.4.2.1](#)), only studies that assessed pain as a primary outcome were further assessed. Similarly, four RCTs were not further considered as the pain outcomes were not assessed in primary analyses. Thus, a total of 35 studies, all RCTs, were considered in the quality of evidence ratings. Overall, these RCTs assessed a total of seven outcomes: (1) Visual Analog Scale (VAS) Pain score; Spontaneous Pain VAS score; (2) Numerical Rating Scale (NRS) Pain score; Body Pain Category Rating Scale (CRS); (3) Other pain scores [Sum of Pain Intensity Differences (SPID); Brief Pain Inventory (BPI); Pain at Present; McGill Pain Questionnaire; Edmonton Symptom Assessment System (ESAS) Pain]; (4) Neuropathic-Specific Pain

scores [Neuropathic Pain Scale; Intensity of Global Neuropathic Pain NRS; Fibromyalgia impact score (pain)]; (5) Sleep Quality [Sleep quality NRS; Sleep disturbance NRS; Sleep disruption NRS]; (6) Pain Disability Index; and (7) Opioid composite score.²¹ Of these, there were two outcomes that met all protocol-specified criteria to undergo meta-analysis calculations: VAS Pain scores and NRS Pain scores. The types of pain spanned across clinical contexts such as multiple sclerosis, post-operative pain, neuropathic pain, chronic pain, and fibromyalgia. Formulations of marijuana administered included smoked, oromucosal sprays, and oral forms.

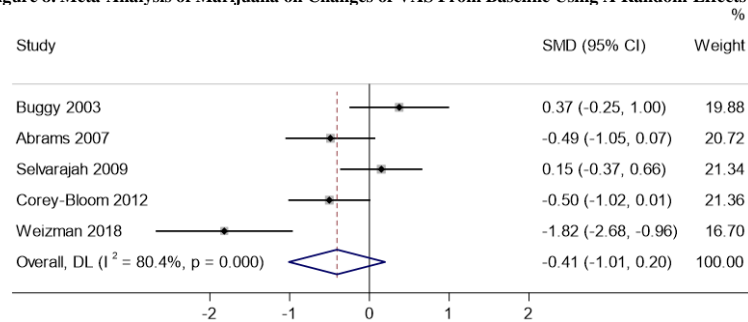
Summary of Effectiveness for Pain

VAS as Primary Outcome

Twelve RCTs were reviewed with a primary outcome of pain measured on the VAS. Six of these studies reported improvement with administration of marijuana and six showed no significant difference when compared to a control. Among the 12 RCTs, five were identified to have homogeneity in assessment strategy and calculation method, and thus were sufficient to calculate meta-analytic estimates. Each of the studies discussed in this section measure change in the pain score from baseline by calculating standard mean difference in VAS. A random effects model was selected and a meta-analysis for standard mean difference (SMD) in VAS was performed. Overall, findings from the pooled analysis trended towards favoring a treatment effect for marijuana over control; however, pooled estimates were not statistically significant (Figure 8). The reported heterogeneity metric, I^2 , suggests that a high (80.4%) proportion of variance in the findings may be due to heterogeneity in the examined studies, and that the accompanying p-value ($p < 0.001$) suggests confidence in this assessment of heterogeneity, but this p-value has limited utility. Thus, there was significant heterogeneity present between the studies included in this meta-analysis and the pooled estimate from these studies may not be representing a true effect of marijuana.

Overall, findings were favoring treatment with marijuana over control; however, pooled estimates were not statistically significant.

²¹ This score captures the quantity of opioid medications used for pain control.

Figure 8. Meta-Analysis of Marijuana on Changes of VAS From Baseline Using A Random-Effects Model²²

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.
 Note: Weights are from random-effects model.

A funnel plot for these studies was also constructed (Figure 9). Most studies fell within the pseudo 95% confidence limits with a notable outlier. The asymmetry in the funnel plot may be indicative of publication bias and/or heterogeneity in the studies assessing this outcome.

²² The p-value reported in the figure is in reference to the accompanying heterogeneity metric I^2

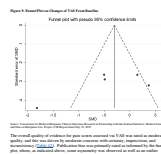


Table 42: Quality of Evidence Rating for Pain Scores Assessed Via Visual Analog Scales, Certainty Rating by Study and Overall					
Overall Certainty					
Domain Assessed	Cohen-Blumen et al. 2012	O'Quinn et al. 2010	Abrams et al. 2007	Shaw et al. 2003	Schwartz et al. 2010
Continuity	Low concern	Moderate concern	Low concern	Low concern	Moderate concern
Imprecision	Low concern	High concern	Low concern	Moderate concern	Low concern
Inconsistency					
Generalizability	High concern	High concern	High concern	High concern	High concern
Publishing bias					
Overall quality of evidence rating					Moderate quality

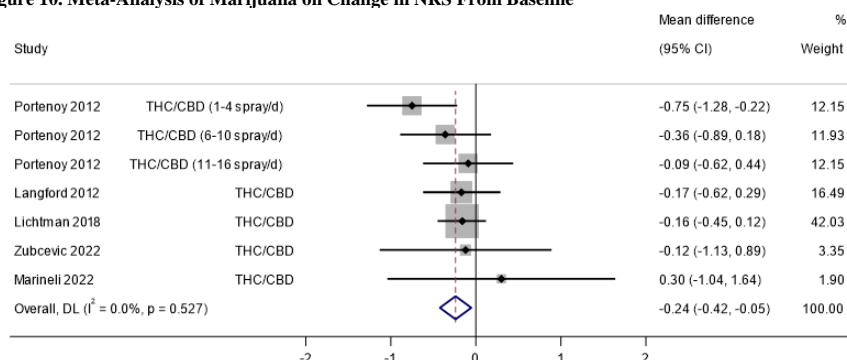
Source: Confidential for Medical Marijuana Clinical Outcome Research in Partnership with the Institute for Health, Medical Cannabis and Data in Marijuana Use Project 2/18 Report dated July 11, 2023.

NRS as Primary Outcome

Eleven RCTs that assessed NRS pain outcomes were included in the review. Two reported improvement, one reported worsening of pain, and eight reported no change when compared to a control group. Five of the studies reported change in NRS from baseline with sufficient homogeneity to allow a calculation of a pooled estimate. Of these five studies, one assessed marijuana's effect for three different dosing regimens, and all dosing regimens were included in the pooled estimates.

A random effects model was selected and meta-analysis for change in NRS from baseline was performed, with results in the figure below (Figure 10). Overall, findings were favoring treatment with marijuana over control. The reported heterogeneity metric, I^2 , suggests that essentially no (0.0%) variance in the findings may be due to heterogeneity in the examined studies, but the accompanying p-value ($p=0.527$) suggests this assessment of heterogeneity may not be informative as it was not statistically significant.

Figure 10. Meta-Analysis of Marijuana on Change in NRS From Baseline²³



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Cannabis Use. Project 2/1B Report dated July 7, 2023.
Note: Weights are from random-effects model.

A funnel plot for these studies was also constructed (Figure 11). All studies assessing pain via NRS fell within the pseudo 95% confidence limits. The asymmetry in the funnel plot may be indicative of publication bias and/or heterogeneity in the studies assessing this outcome.

²³ The p-value reported in the figure is in reference to the accompanying heterogeneity metric I^2

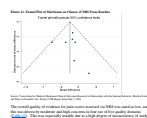


Table 43. Quality of Evidence Rating for Pain Scores Assessed Via Numeric Rating Scales, Certainty Rating by Study and Overall

Domain Assessed	Perrone et al. 2012	Hawford et al. 2012	Gschman et al. 2016	Zolbec et al. 2012	Morinelli et al. 2012	Overall Certainty Rating Across Studies Assessing That Outcome
Internal validity	Low concern	Moderate concern	Moderate concern	Low concern	Moderate concern	Moderate concern
External validity	Moderate concern	Low concern	Low concern	Moderate concern	Moderate concern	Moderate concern
Imprecision						Moderate concern
Inconsistency						High concern
Generalizability	High concern	High concern	High concern	High concern	High concern	High concern
Publication bias						Low concern
Overall quality of evidence rating						Low quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sanntet Initiative. Medical Literature and Data on Cannabis Use. Project 21B Report dated July 7, 2023.

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Table 44. Quality of Evidence Rating for Pain Scores Via Other Types of Patient-Reported Scores or Questionnaires, Certainty Rating by Study and Overall

Overall Certainty Rating Across Studies Assessing That Outcome				
Domain Assessed	(Gruny et al. 2002)	(Langford et al. 2012)	(Jefferson et al. 2013)	(Binks et al. 2006)
Certainty	Low concern	Moderate concern	High concern	High concern
Imprecision	Moderate concern	Low concern	Moderate concern	Moderate concern
Inconsistency				Low concern
Generalizability	High concern	High concern	High concern	High concern
Publication bias				Low concern
Overall quality of evidence rating				Low quality

Source: Commission for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentient Initiative. Medical Literature and Data on Cannabis Use. Project 110 Report dated July 7, 2023.



Table 4E: Quality of Evidence Rating for Pain Scores Assessed Via Neurospinal-Specific Pain Scales, Certainty Rating by Study and Overall

Domain Assessed	(Nussli et al. 2012)	(Wilson et al. 2012a)	(Gibson et al. 2012)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Low concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Low concern	Moderate concern	Moderate concern
Inconsistency				Moderate concern
Generalizability	High concern	High concern	High concern	High concern
Publishability bias				Low concern
Overall quality of evidence rating				Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Scottish Initiative: Medical Literature and Data on Cannabis Use. Report 2.0 Report dated July 5, 2023.

[\[REDACTED\]](#)

Table 46. Quality of Evidence Rating for Sleep Quality in People With Pain, Certainty Rating by Study and Overall

Domain Assessed	(Nurmikko et al. 2007)	(Lackmann et al. 2018)	(Lundford et al. 2015)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern	Moderate concern	Moderate concern
Imprecision	Moderate concern	Low concern	Low concern	Moderate concern
Inconsistency				Moderate concern
Generalizability	High concern	High concern	High concern	High concern
Publication bias				Low concern
Overall quality of evidence rating				Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Scottish Initiative, Medical Literature and Data in Cannabis Use, Project 2718 Report Zined July 7, 2023.

There was one RCT assessing pain disability index as an outcome. The quality of evidence rating is shown in [Table 47](#).

Table 47. Quality of Evidence Rating for Pain Disability, Certainty Rating by Study and Overall

Domain Assessed	(Nurmikko et al. 2007)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	High concern	High concern
Publication bias		Low concern
Overall quality of evidence rating		Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Cannabis Use. Project 2/1B Report dated July 7, 2023.

Opioid composite score was an identified outcome in one RCT. The study assessing the opioid composite score outcome investigated three different dosing regimens of marijuana as compared with placebo. The results were mixed across the three comparator groups. The overall quality of evidence was rated as moderate ([Table 48](#)).

Table 48. Quality of Evidence Rating for Opioid Composite Score, Certainty Rating by Study and Overall

Domain Assessed	(Portenoy et al. 2012)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Low concern	Low concern
Imprecision	Moderate concern	Moderate concern
Inconsistency		Unable to rate
Generalizability	High concern	High concern
Publication bias		Low concern
Overall quality of evidence rating		Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Cannabis Use. Project 2/1B Report dated July 7, 2023.

Overall UF Effectiveness Conclusions for Pain

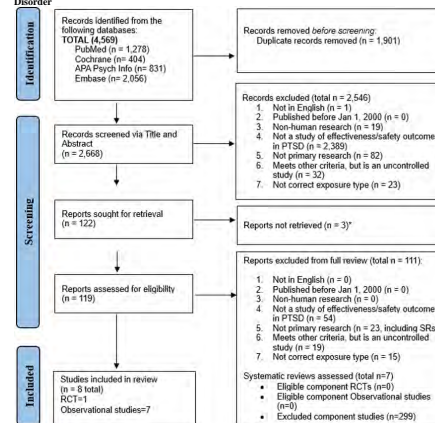
The evidence for improvement of pain disability was rated as moderate quality based on one RCT. The evidence for pain scores and opioid composite scores were also rated as moderate quality, but findings were mixed or inconclusive across studies. The evidence for other pain scores, sleep quality, and other quality of life outcomes was rated as low quality, but findings were mixed across studies, with some reporting improvements and many reporting inconclusive findings, but none reporting worsening. The meta-analyses performed were based on studies that were able to be combined for analysis, which does exclude some of the studies reviewed due to design differences. Although there was a trend towards benefit for VAS scores for marijuana, it did not reach significance in five of the combined studies that assessed this outcome. Additionally, the meta-analysis for the NRS outcome did show a small but statistically significant benefit (SMD -0.24) based on a low quality of evidence.

Summary of Safety for Pain

There was a limited amount of information reported with respect to safety. Overall, more participants reported AEs when treated with marijuana than those treated with an active

[illegible]

Figure 12. PRISMA Flow Diagram Documenting Attrition (Exclusions) for Post-Traumatic Stress Disorder



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinal Initiative. Medical Literature and Data on Cannabis Use. Project 2-18 Report dated July 7, 2023.

Six of the seven observational studies eligible for inclusion were rated as having a critical risk of bias and were not considered further. Thus, the final systematic review included an RCT and an observational study, both with the Clinician-Administered PTSD Scale for Diagnostic and Statistical Manual of Mental Disorders (CAPS-5) assessment as the outcome. The quality of evidence rating for the two studies for the CAPS-5 outcome is shown in [Table 49](#).

Table 49. Quality of Evidence Rating for the PTSD Severity Assessment Outcome (CAPS-5), Certainty Rating by Study and Overall

Domain Assessed	(Bonn-Miller et al. 2021)	(Bonn-Miller et al. 2022)	Overall Certainty Rating Across Studies Assessing That Outcome
Certainty	Moderate concern	Moderate concern	Moderate concern
Imprecision	High concern	Moderate concern	High concern
Inconsistency			Moderate concern
Generalizability	Low concern	Low concern	Low concern
Publication bias			Low concern
Overall quality of evidence rating			Moderate quality

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Cannabis Use. Project 2/1B Report dated July 7, 2023.

As specified in the protocol, these two studies did not meet thresholds for the minimum number of studies to qualify for meta-analysis calculation.

Summary of Effectiveness for PTSD

The single identified RCT evaluated short-term impact of three formulations of smoked marijuana and found all treatment groups (placebo, High CBD, High THC, THC+CBD) achieved statistically significant reductions in PTSD severity on the CAPS-5; however, the study did not find a significant difference in change in PTSD symptom severity between the active cannabis concentrations and placebo.

The prospective observational study conducted in Colorado residents with PTSD ages 18 years or older showed that, over the course of a year, the group using cannabis reported a more significant reduction in PTSD symptom severity over time compared to the control group not using cannabis.

The evidence for this outcome 'PTSD severity' was rated by the UF investigators as moderate quality.

Summary of Safety for PTSD

Within the single RCT, the most common AEs reported (i.e., those with >10% frequency) were cough (12.3%), followed by throat irritation (11.7%), and anxiety (10.4%). Three SAEs were reported and determined to be unrelated (heart palpitations, pulmonary embolism, and abscess). The number of participants who reported an AE did not differ significantly from placebo.

The observational study did not examine safety outcomes.

4.3. Conclusions Based on the Report by the University of Florida

UF concluded there is low to moderate quality evidence supporting efficacy²⁴ of marijuana as medical treatment for outcomes in several indications, including anorexia, nausea and vomiting, and PTSD. UF performed meta-analyses for VAS and NRS outcome measures in the pain indication, based on studies with sufficient homogeneity

²⁴ The systematic reviews largely relied on RCTs as there were only two observational studies included in the quality of evidence assessments: one for the anxiety indication and one for the PTSD indication.

and where the quality of evidence was considered at least moderate. UF concluded that pooled VAS reported outcomes trended towards showing a benefit for marijuana but did not reach statistical significance when compared to a control group. The results for the pooled NRS reported outcomes showed a small but significant difference when compared to a control group. Although a large literature base was identified for the pain indication, with a number of RCTs showing benefit and their meta-analysis showing a small but significant effect for marijuana on the NRS outcome measure, UF concluded the data were too inconsistent to provide a conclusive statement on the benefit of marijuana for the treatment of pain.

The UF report summarized the limited available safety data contained in the published reports. FDA did not identify any safety concerns described in the UF report that would indicate the medical use of marijuana poses unacceptably high safety risks for the indications evaluated for its therapeutic effect.

4.4. FDA Review of Published Systematic Reviews and Meta-Analyses

As a part of the assessment of CAMU, FDA also conducted a separate review of published systematic reviews and meta-analyses of botanical forms of marijuana and those results are discussed below. This was a high-level review of the literature assessing the effectiveness and safety of these forms of marijuana on the identified indications based on Part 1 of the CAMU test and in the informal landscape analysis performed by FDA. This portion of our review is intended to compare the findings from UF's review with other experts in the field. The most commonly identified forms in the literature included nabiximols oromucosal spray,²⁵ inhaled marijuana (whole plant or plant-derived), and botanically derived marijuana extracts. Within this section, we examined reviews including The National Academies of Sciences, Engineering, and Medicine (NASEM) Comprehensive Review of the Health Effects of Using Cannabis and Cannabis-Derived Products (2017), the Living Systematic Review on Cannabis and Other Plant-Based Treatments for Chronic Pain by the Agency for Healthcare Research and Quality (AHRQ), as well as identified published systematic reviews and meta-analyses relevant to this document.

4.4.1. Sources of Review

The National Academies of Sciences, Engineering, and Medicine (NASEM)

The NASEM report (2017) consists of a comprehensive review of evidence regarding the health effects of using cannabis and cannabis-derived products. The NASEM report covered a broader range of products, inclusive of all cannabinoids, in contrast to our review, which focuses on marijuana. For purposes of this summary, we will only focus

²⁵ Nabiximols (brand name Sativex in countries where it is approved) is a botanically derived oromucosal spray consisting of 2.7 mg of THC and 2.5 mg of CBD per spray. Nabiximols has been approved for the treatment of spasticity due to multiple sclerosis in the United Kingdom since June 2010.

on the NASEM report's findings for forms that fall under the definition of marijuana. A section of the NASEM report summarized potential therapeutic uses of marijuana based on a literature search, evidence review, grading, and synthesis of information. The committee's conclusions are based on the findings from published systematic reviews. Where no systematic review existed, the committee reviewed all fair and good-quality relevant primary research published between January 1, 1999, and August 1, 2016. Primary research was assessed using standard approaches (e.g., Cochrane Quality Assessment, Newcastle–Ontario scale) as a guide. The committee weighed the evidence and placed conclusions into one of five categories in decreasing order of strength of evidence: Conclusive, substantial, moderate, limited and insufficient. The standard of some credible scientific support required for our review would appear to be consistent with at least the limited strength of evidence standard in the NASEM report.

Agency for Healthcare Research and Quality (AHRQ)

The AHRQ is conducting a living systematic review on cannabis and other plant-based treatments for chronic pain that includes randomized controlled trials and comparative observational studies with a minimum of 4 weeks duration for noncancer chronic pain in adults. Cannabinoid interventions were categorized according to their THC-to-CBD ratio (comparable, high, low) and according to the source of the compound (whole-plant, extracted from whole-plant, or synthetic). Strength of evidence was assessed as low, moderate, high, or insufficient, and magnitude of effect was assessed. The living review is updated on a quarterly basis.

FDA Review of Systematic Reviews and Meta-Analyses

We conducted our own high-level analysis of published systematic reviews and meta-analyses over the past 10 years to evaluate the potential evidence for a therapeutic effect for marijuana, as well as its potential harms when used in this context. Although the primary research covered by each review (i.e., AHRQ, NASEM, UF review, our review of systemic reviews and meta-analyses) overlapped with one another, the purpose of our review was to analyze several groups' conclusions on the data for each of the selected indications, if available.

For the purposes of this analysis, we focused on those studies or treatment arms relevant to marijuana. If the formulation of the marijuana product could not be determined, FDA attempted to review the individual source studies. Of note, the majority of AE data were accumulated mostly from studies that evaluated pain. Therefore, any pooled analysis of AEs across indication will be discussed in the pain section (Section [II.4.4.1.1](#)), and AE data will only be discussed in other sections if there was a dedicated evaluation of AE data in that specific indication.

4.4.1.1. Pain

The mechanism of marijuana's effect on pain relief is not fully clear; however, there is some evidence from experimental pain studies in healthy subjects that all cannabinoids may prevent pain through small increases in pain thresholds and making pain feel less

unpleasant through altering the affective processes as opposed to reducing pain intensity already experienced ([De Vita et al. 2018](#)).

NASEM Report Conclusions and Highlights

The NASEM report (2017) stated there is substantial evidence for treatment of chronic pain in adults with cannabis ([NASEM 2017](#)). This determination was based on mostly plant-derived formulations. The relevant information from this report as it pertains to our analysis of marijuana is described in this section.

One systematic review cited in this report ([Whiting et al. 2015](#)) evaluated studies across numerous types of chronic pain (e.g., cancer pain, diabetic peripheral neuropathy) and NASEM heavily factored these findings into their conclusions. The Whiting (2015) publication included a total of 22 trials of plant-derived cannabinoids (thirteen studies with nabiximols; five trials of plant flower smoked or vaporized form, three trials of THC oramucosal spray; and one trial of oral THC). Whiting (2015) performed an analysis across seven trials that evaluated the effects of nabiximols and one that evaluated the effects of inhaled cannabis, which suggested plant-derived cannabinoids increased the odds for improvement of pain by approximately 40 percent versus the control condition (odds ratio [OR], 1.41, 95% confidence interval [CI] = 0.99-2.00; eight trials). One notable study showing efficacy (N = 50) examined inhaled vaporized cannabis and was included in the effect size estimates. This single study (Abrams, 2007) showed that cannabis reduced pain versus a placebo (OR, 3.43, 95% CI = 1.03–11.48).

The NASEM report noted the effect size for inhaled cannabis observed with the Abrams (2007) study is consistent with another meta-analysis of five trials which studied the effect of inhaled cannabis on neuropathic pain ([Andreae et al. 2015](#)). The pooled OR from these trials showed a pooled effect estimate of 3.22 for pain relief versus placebo (95% CI = 1.59–7.24) tested across nine THC concentrations ([Andreae et al. 2015](#)). Of note, two of the primary studies included in this review by Andreae (2015) were also included in the Whiting (2015) review.

In the addition to the reviews above ([Andreae et al. 2015](#); [Whiting et al. 2015](#)), the NASEM report identified two additional primary studies which examined the effect of cannabis flower on acute pain ([Wallace et al. 2015](#); [Wilsey et al. 2016a](#)). NASEM concluded that these two studies have consistent findings with the meta-analyses described above, suggesting a reduction in pain after cannabis administration, and thus contributed to NASEM's conclusion of substantial evidence of efficacy.

AHRQ Conclusions and Highlights

The AHRQ reviewed and summarized randomized controlled trials (mostly placebo controlled) of patients with chronic pain (mostly neuropathic in origin) with treatment duration between four weeks and less than 6 months ([AHRQ 2023](#)). The AHRQ determined that oral sprays containing comparable amounts of THC and CBD (e.g., nabiximols) are “probably associated with small improvements in pain severity and overall function,” but there may be a large increased risk of dizziness and sedation with moderate risk of nausea. Evidence on whole-plant cannabis, low-THC-to-CBD ratio products, other cannabinoids, or comparators with other active interventions was insufficient to draw conclusions. Overall, the AHRQ has determined thus far that “select

individuals with chronic neuropathic pain may experience moderate short-term improvements in pain when using cannabis products [(synthetic or extracted from whole-plant)] that have a high-THC to CBD ratio.” Additionally, cannabis with a comparable amounts of THC and CBD may result in small improvements in pain severity with increased AEs when the THC-to-CBD ratio is higher.

FDA Review of Systematic Reviews and Meta-Analyses

These reviews covered a number of routes of administration (e.g., oromucosal, smoked) and product types. The content below is separated by each respective route of administration or product type for ease of review.

There have been a number of studies completed using nabiximols to treat pain associated with multiple sclerosis and other pain-related conditions (i.e., neuropathic pain), that demonstrated findings of efficacy ranging from inconclusive to a moderate beneficial effect. Nabiximols has been shown in meta-analyses to demonstrate a modest benefit in chronic neuropathic pain where the NRS was assessed and the evidence was determined to be of moderate quality ([Whiting et al. 2015](#); [Meng et al. 2017](#)). Specifically, one meta-analysis of six chronic neuropathic pain trials (Meng, 2017) revealed a significant but clinically small reduction on the 11-point pain NRS with nabiximols when compared to placebo in patients with neuropathic pain (mean difference -0.50 points; 95% CI, -0.89 to -0.12 points; $P = 0.010$) with some evidence of heterogeneity between studies ($I^2 = 43\%$). Another meta-analysis ([Whiting et al. 2015](#)) of six chronic neuropathic pain trials reached a similar conclusion showing a greater average reduction in the NRS assessment of pain for marijuana (weighted mean difference [WMD], -0.46 [95% CI, -0.80 to -0.11]) with no evidence of heterogeneity ($I^2=0\%$). A number of authors of systematic reviews and meta-analyses have concluded that nabiximols may be considered as an adjunct analgesic in neuropathic pain, with a benefit ranging from weak to moderate effect in a number of neuropathic pain conditions ([Meng et al. 2017](#); [Nielsen et al. 2018](#); [Stockings et al. 2018a](#); [Bilbao and Spanagel 2022](#)).

Another common route of marijuana administration is via the inhalation route (i.e., smoked or vaped). One meta-analysis of inhaled cannabis, supplied by the NIDA, that consisted of five randomized, placebo-controlled, double-blind trials in numerous types of neuropathic pain (e.g., HIV neuropathy, diabetic neuropathy, complex regional pain) with treatment up to two weeks of dosing provided evidence of benefit ([Andreae et al. 2015](#)). The estimated OR for a more than 30% reduction in pain scores in response to inhaled cannabis versus placebo for chronic painful neuropathy was 3.2 with a Bayesian 95% credible interval [1.59, 7.24], and the number needed to treat as 5.55. Additionally, the data showed effect increased with THC content. Based on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) definition of at least moderate benefit (OR 3.1), this meta-analysis suggested a moderate benefit for inhaled cannabis. The authors concluded the studies in their analysis were of mostly good quality and homogenous across studies. However, the nature of the intervention likely interfered with effective blinding which may have resulted in high risk of performance bias and possible detection bias. A more recent meta-analysis pooled eight clinical studies assessing inhaled cannabis (five smoked and three vaporized) versus placebo in patients with chronic pain ([Wong et al. 2020](#)). This meta-analysis showed inhaled cannabis was

associated with statistically significant analgesic effect, with a mean difference of -0.97 ($p < 0.001$, random effect) on the NRS; however, significant heterogeneity was identified ($I^2 = 58.4\%$). Additionally, a further subgroup analysis showed no difference in effect between smoked or vaporized forms. Other systematic reviews similarly concluded a moderate level of benefit for inhaled cannabis in the neuropathic pain population ([Deshpande et al. 2015](#); [Lynch and Ware 2015](#); [Nabata et al. 2021](#)).

Cannabis extracts derived from *Cannabis sativa* are another form of marijuana used to treat pain conditions. In a meta-analysis of studies using cannabis extract in patients with multiple sclerosis, pooled data showed statistical significance for cannabis extract with a small effect size of -0.33 (-0.50 to -0.16), which indicated a small-moderate clinical effect of the treatment with no evidence of heterogeneity between analyzed studies ([Torres-Moreno et al. 2018](#)). A recent meta-analysis of six chronic neuropathic pain trials assessing cannabis extracts versus placebo with THC at varying strengths (1% to 9.4%) showed significant improvement in pain intensity by -8.7 units on a 0-100 scale ($P < .001$) based on a moderate quality of evidence ([Sainsbury et al. 2021](#)). Within this meta-analysis, the authors also showed pooled data from five of the studies that included reports on response rates and showed that patients receiving cannabis extract were 1.855 times more likely to achieve a 30% reduction in pain than patients in the placebo group ($P < .001$).

Other systematic reviews and meta-analyses showed limited to no appreciable effect in some pain groups such as cancer-related pain and spinal cord injuries ([Fitzcharles et al. 2016](#); [Boland et al. 2020](#); [Tsai et al. 2022](#); [Barakii et al. 2023](#)). When attempting to identify whether cannabis may have an opioid-sparing effect, the data showed any effect was uncertain ([Noori et al. 2021](#)) or there was likelihood of an effect, but a causal inference could not be determined ([Okusanya et al. 2020](#)). A lack of evidence of efficacy was also shown in the acute post-operative period in a meta-analysis of all cannabinoids (botanical and synthetic) and notably an increased risk of hypotension with an OR of 3.24 ([Abdallah et al. 2020](#)). In contrast, recently published Canadian clinical practice guidelines ([Bell et al. 2023](#)) identified observational studies with a positive association between cannabis use and opioid sparing and made a strong recommendation based on moderate-quality evidence for the use of cannabis-based medicines among people using moderate/high doses of opioids (> 50 morphine equivalents) for the management of chronic pain and/or increase opioid sparing.

In general, the adverse event profile of marijuana has been well-characterized based on years of clinical studies, observational studies, and harms data. The systematic reviews and meta-analyses did not reveal any new safety signal. It is clear that adverse events are more common in marijuana groups when compared to placebo control and are also a considerable reason for the risk of bias in studies due to potential unmasking of the treatment group. Adverse events commonly identified consisted of anxiety, dry mouth, tiredness, drowsiness, dizziness, nausea, diarrhea, constipation, and euphoria in the mild to moderate range of severity with serious adverse events generally uncommon ([Deshpande et al. 2015](#); [Lynch and Ware 2015](#); [Whiting et al. 2015](#); [Meng et al. 2017](#); [Torres-Moreno et al. 2018](#); [Wong et al. 2020](#); [Sainsbury et al. 2021](#)). In general, no differences in adverse events were identified between types of cannabinoids or mode of administration ([Whiting et al. 2015](#); [Torres-Moreno et al. 2018](#)). For example, one meta-

analysis noted when compared with placebo groups, patients receiving cannabinoids were more likely to report individual adverse events such as dizziness (OR 5.52, 95% CI 4.47-6.83), cognitive attention or disturbance (OR 5.67, 95% CI 2.72-11.79), and confusion and disorientation (OR 5.35, 95% CI 2.31-12.3) when pooling safety data for all types of cannabinoids (Stockings et al. 2018a). One systematic review also showed adverse events were consistently identified in a number of pain indications, and individuals who are experienced with cannabis use have a reduced risk of adverse events likely due to development of tolerance (Allan et al. 2018). Dosing varied per study, and dose optimization cannot be determined from the available literature. However, it has been suggested that self-titrating cannabis through inhalation may result in more potent dosages (Price et al. 2022).

A recently published clinical practice guideline concluded with a strong recommendation based on moderate-quality of evidence for the use of cannabis-based medicines (includes synthetic forms, CBD alone, and botanical) in chronic pain as a monotherapy, replacement, or adjunct treatment (Bell et al. 2023). This conclusion was based on a number of controlled-studies, systematic reviews, meta-analyses, and observational studies. Although these findings are not specific to botanically-derived marijuana, they draw a conclusion that either the key elements of marijuana, or marijuana itself, is beneficial for chronic pain.

Our review of published systematic reviews and meta-analyses shows most authors concluded there is some benefit with marijuana in the treatment of pain conditions, generally ranging from low to moderate effect based on low to moderate quality of evidence.

4.4.1.2. Anxiety Disorders

There is a lack of high-quality studies examining marijuana in the treatment of anxiety. THC has psychoactive effects that include an anxiogenic response, whereas CBD is associated with anxiolytic properties (de Almeida and Devi 2020; Sharpe et al. 2020). However, there is some very low-quality evidence that synthetic THC and nabiximols may lead to small improvement in anxiety symptoms in patients with other medical conditions such as multiple sclerosis and chronic non-cancer pain (Black et al. 2019).

There is also data from a meta-analysis (Hindley et al. 2020) to indicate that synthetic and botanical forms of THC worsen general psychiatric symptoms such as depression and anxiety when compared to placebo with a large effect size (1.01 [95% CI 0.77-1.25], $p < 0.0001$). Another systematic review suggested THC (includes both synthetic and botanically derived forms) worsened or caused anxiety symptoms and showed little benefit in several psychiatric disorders (Stanciu et al. 2021).

Based on the available literature, there is not any good evidence to suggest marijuana is an effective treatment of anxiety. Alternatively, it appears the THC component of marijuana is more likely to have anxiogenic effects rather than benefit.

4.4.1.3. Nausea and Vomiting

The most common reason patients with cancer use cannabis and cannabinoids is for the relief of nausea and vomiting ([Sawtelle and Holle 2021](#)). Most studies evaluated nausea and vomiting related to cancer, and if specified, as a complication of chemotherapy. Systematic reviews and meta-analyses were identified but the vast majority of information relates to synthetic forms of THC (i.e., dronabinol, nabilone and levonantranol). This is not surprising given synthetic oral formulations have FDA approval for chemotherapy-induced nausea and vomiting (e.g., nabilone and dronabinol). For example, the NASEM report (2017) only provided a conclusion relating to the oral cannabinoid preparations nabilone and dronabinol (conclusive evidence of effectiveness) ([NASEM 2017](#)).

As stated above, the vast majority of studies evaluated synthetically derived Δ^9 -THC. A number of older studies from the mid-1970s to 1980s showed significant benefit, but have methodological limitations compared to more recent studies, and it should be noted these older studies were conducted prior to the availability of more modern effective antiemetics ([Sawtelle and Holle 2021](#)). A systematic review concluded there was a low-quality of evidence that cannabinoids (including nabiximols and synthetic THC) were associated with improvements in nausea and vomiting due to chemotherapy ([Whiting et al. 2015](#)). A recent meta-analysis did not show nabiximols was better than placebo for nausea and vomiting ([Bilbao and Spanagel 2022](#)). However, other systematic reviews suggested cannabinoids show a clinically meaningful improvement compared with placebo in patients with nausea and vomiting after chemotherapy; however, the findings appear to be based mostly on synthetically-derived Δ^9 -THC ([Allan et al. 2018](#); [Montero-Oleas et al. 2020](#)).

4.4.1.4. Post-Traumatic Stress Disorder

Although there is some observational data suggesting people with PTSD self-treat with cannabis ([Bonn-Miller et al. 2014a](#); [Bonn-Miller et al. 2014b](#)), there is limited high quality, controlled clinical trial data available on marijuana and PTSD. A systematic review concluded there is some association of a reduction in PTSD symptoms measured by psychometric outcomes and improved quality of life, but this finding was based on observational studies with a high risk of bias ([Rehman et al. 2021](#)). This same review concluded that the most common adverse effects reported were dry mouth, headaches, psychoactive euphoria and agitation, and palpitations but that cannabinoids (numerous formulations studied including synthetic THC, CBD, unknown formulations) were overall well-tolerated. A recent systematic review identified two cohort studies, one retrospective and one prospective, which provided some evidence of benefit of cannabinoids but not specific to marijuana ([Forsythe and Boileau 2021](#)). Specifically, the retrospective analysis evaluated Clinician Administered Post-traumatic Scale for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (CAPS) scores prior to entering a medical cannabis program in New Mexico and then a second score after being enrolled and treated ([Greer et al. 2014](#)). A significant decrease ($p < 0.0001$) in CAPS scores was observed from before and after cannabis use, from 98.8 ± 17.6 (mean \pm SD) to 22.5 ± 16.9 , indicating a reduction in overall PTSD symptoms. The identified

prospective cohort study evaluated THC in patients with chronic PTSD in ten patients (Roitman et al. 2014). There was a significant decrease in specific symptoms of PTSD: Clinical Global Impression-Improvement Scale (3.5 ± 0.52 to 2.7 ± 1.25 , $p < 0.03$), hyperarousal (32.3 ± 4.73 to 24.3 ± 9.11 , $p < 0.02$), sleep quality (17.20 ± 2.65 to 13.9 ± 4.48 , $p < 0.05$), frequency of nightmares (0.81 ± 0.55 to 0.44 ± 0.41 , $p < 0.04$), and total Nightmare Effects Survey (NES) scores (32.2 ± 11.29 to 22.9 ± 8.7 , $p < 0.002$). The above studies reported marijuana was well-tolerated with mild AEs (e.g., dry mouth, dizziness).

The NASEM report (2017) did not identify any evidence for treatment of PTSD with a botanically-derived form of marijuana and concluded there is limited evidence of effectiveness for any cannabinoid (NASEM 2017). The only evidence NASEM identified for any THC product in this condition was a small study which administered synthetic THC (nabilone). Other systematic reviews also concluded there was insufficient evidence to draw a conclusion or support use of plant-based forms of marijuana (O'Neil et al. 2017; Shishko et al. 2018; Hindocha et al. 2020; Jugl et al. 2021).

Overall, there is a lack of quality clinical data to support the use of marijuana for PTSD. Evidence of benefit was based mostly on case-reports and observational studies with high risk of bias.

4.4.1.5. Inflammatory Bowel Disease

Numerous survey data suggest marijuana has patient-reported improvement in symptoms of IBD suggesting potential benefit as a treatment option in this population (Norton et al. 2017; Desmarais et al. 2020; Doeve et al. 2021). A number of reviews, including meta-analyses, have been performed and are described below. Given the small number of studies performed, there is overlap in studies across these reviews. However, review of different authors' analyses are intended to provide further insights into the available data.

A systematic review of Cochrane Database systematic reviews identified three studies that assessed cannabis in patients with active Crohn's disease and two studies in patients with ulcerative colitis (Kafil et al. 2020). The studies were small with varying THC/CBD ratios. Two of the Crohn's disease trials assessed botanically derived marijuana products (smoked cannabis and sublingual cannabis oil) and showed induction of remission was greater in the cannabis groups compared to placebo. The smoked cannabis study showed that a clinical response (defined as a 100-point Crohn's Disease Activity Index (CDAI) reduction from baseline) at eight weeks was reported in 91% (10 of 11) of participants in the treatment group compared with 40% (4 of 10) of participants in the placebo group (relative risk [RR] 2.27; 95% CI, 1.04-4.97;) with a very low certainty of evidence and high risk of bias. The second study administered cannabis oil (4% THC) for eight weeks and showed the mean quality of life score was 96.3 in the cannabis oil group compared with 79.9 in the placebo group (mean difference 16.40; 95% CI, 5.72-27.08, low certainty evidence). In addition, the mean CDAI score at 8 weeks was 118.6 in the cannabis oil group compared with 212.6 in the placebo group (mean difference -94.00; 95% CI, 148.86-39.14, low certainty evidence). Two randomized trials were identified in ulcerative colitis patients and the authors concluded there was no firm evidence to support efficacy or safety of cannabis use in patients with active ulcerative colitis.

Adverse events in the above studies included dizziness, headache, sleepiness, dry mouth, fatigue, and nausea. There did not appear to be any serious adverse events related to marijuana treatment. The authors concluded that there is low to very low certainty of evidence of efficacy and no firm conclusion could be made due to limitations of the studies, such as small sample sizes.

A recent meta-analysis of the available studies utilizing botanically derived oil or dried plant marijuana products for smoking or oral administration showed some benefit in Crohn's disease [pooled risk-ratio 0.42 (-0.04, 0.890)] coming close to statistical significance with a low degree of heterogeneity in studies ([Vinci et al. 2022](#)). Also, mean CDAI reduction was greater in patients treated with marijuana products than with placebo (mean CDAI reduction of 36.63, CI 95% 12.27-61.19). This same meta-analysis did not find benefit based on the ulcerative colitis pooled data. The authors concluded marijuana as an adjuvant therapy may improve Crohn's Disease symptoms, but the studies had numerous limitations including small sample sizes. Another meta-analysis of available data did not show any benefit of marijuana with regard to remission status or a clinical response when compared to placebo in IBD, but the authors suggested there may be a role as an adjunct to standard therapy ([Desmarais et al. 2020](#)).

Another analysis of available randomized control studies and observational studies showed cannabis products do not induce remission in IBD ([Doeve et al. 2021](#)). The majority of interventional products in this review were botanically derived. A meta-analysis did not show any statistically significant benefit with remission status [RR 1.56 (0.99, 2.46)] but did show significance for perceived efficacy on various Likert-scales [RR 0.61 (0.24, 0.99)]. The authors concluded these types of cannabinoids were not effective in induction of remission but did produce a perceived benefit to patients. They postulate THC's CB1 activity and reciprocal TRPV1 downregulation correlate with improved visceral hypersensitivity and reduced colonic motility, thereby improving abdominal pain, diarrhea, and nausea. Although there was some evidence of a therapeutic benefit, the authors did not reach a firm recommendation and believed a larger randomized-controlled trial is warranted.

Evidence in a systematic review assessing abdominal pain related to IBD was limited to one open-label pilot study and two surveys. These studies showed some possible benefit in short-term pain relief, but these studies have significant limitations such as no control group, significant amount of data relied on survey data, and significant risks of biases ([Norton et al. 2017](#)).

It appears from the available data that there is some evidence of benefit in Crohn's disease when treated with marijuana. However, this appears mostly limited to subjective symptoms and not disease activity. There is no significant evidence to suggest benefit in ulcerative colitis. Some authors recommended marijuana may be useful as an adjunct in Crohn's disease if other options have failed, but a general consensus is more data from large randomized controlled trial(s) are required to provide a firm conclusion with regard to efficacy, safety, and dosing optimization.

4.4.1.6. Epilepsy

Although there is some evidence of efficacy for CBD in reducing seizure activity in pediatric drug-resistant epilepsy in the literature and FDA has approved a product containing highly purified plant-derived CBD for seizures related to specific syndromes (i.e., Lennox-Gastaut epilepsy, tuberous sclerosis, myoclonic epilepsy in infancy), there are not sufficient data to determine that other cannabis-based products (i.e., marijuana) are effective in the treatment of epilepsy, given the lack of quality studies ([Stockings et al. 2018b](#); [Elliott et al. 2019](#); [Elliott et al. 2020](#)). See Section II.4.6 of this document for further information related to Epidiolex and its approval. The 2017 NASEM report also concluded there was insufficient evidence to support or refute a conclusion that cannabinoids, such as marijuana, are effective for epilepsy ([NASEM 2017](#)).

4.4.1.7. Anorexia Related to Medical Conditions

Dronabinol (a synthetic form THC) is FDA approved to treat anorexia associated with HIV. However, data based on botanically derived marijuana are more limited. NASEM reviewed systematic reviews and individual primary literature as well, which included botanically derived marijuana and synthetic THC ([NASEM 2017](#)). The report concluded there is little evidence that cannabis and oral cannabinoids are effective in increasing appetite and decreasing weight loss in the population with HIV and/or acquired immunodeficiency syndrome (AIDS). It was also concluded that there is insufficient evidence to support or refute the conclusion that cannabinoids are an effective treatment for anorexia-cachexia due to cancer.

A systematic review and meta-analysis did not find any high-quality evidence suggesting cannabinoids are beneficial for anorexia or cachexia in cancer or HIV patients ([Whiting et al. 2015](#); [Mucke et al. 2018](#); [Simon et al. 2022](#)). These analyses were based on combined studies of herbal marijuana and plant-derived and synthetic THC; therefore, these analyses are not entirely specific to botanical forms. In addition, one of these reviews included uncontrolled studies in the analysis. Mucke (2018) identified one study comparing herbal marijuana with synthetic dronabinol and noted that both groups gained 3.0 and 3.2 kg, respectively, with no serious AEs reported ([Mucke et al. 2018](#)). Alternatively, another meta-analysis of three studies, including what appeared to be both botanical extracts and synthetic THC, showed a trend towards increased appetite (mean difference 0.27, 95% CI -0.51 to 1.04) when compared with a placebo ([Wang et al. 2019](#)). The Whiting et al. review only identified one study which evaluated weight gain with marijuana and found no benefit when compared with placebo ([Whiting et al. 2015](#)). However, this same analysis showed a trend towards a decrease in quality of life in the two studies which assessed this outcome. The authors hypothesized this trend may be due to adverse events related to marijuana.

In summary, it appears the majority of systematic reviews covered synthetic forms of THC with limited information supporting marijuana's benefit related to this review.

4.5. Safety Data From Case Studies of Selected State Programs: Maryland and Minnesota

The purpose of this section is to describe the number of individuals using marijuana based on medical advice and the safety experience of these patients in states with authorized medical marijuana programs. FDA reviewed results from state reporting data from 37 states with medical marijuana programs and surveys of patients using marijuana in Maryland and Minnesota.

The University of Michigan provided state annual reports for 37 states. The number of patients using marijuana for medical purposes increased every year from 661,990 in 2016 to 2,974,433 in 2020 (Appendix [Table 79](#)). There were no safety data relevant to this review included in these annual reports (i.e., no inferential analyses of epidemiologic data). There was no information provided regarding the quality control processes for data analysis or data management for these results.

We considered patient survey data from Maryland and Minnesota in more depth than the other 35 states because they had available survey data and were able to provide the results and/or data to FDA. Therefore, these two states were used as an approximate representative sample of safety data from jurisdictions with state-legalized use of marijuana for medical purposes.

4.5.1. Maryland

4.5.1.1. Maryland Methods

In 2022, the Maryland Medical Cannabis Commission (MMCC) conducted an online survey of certified medical cannabis patients in Maryland (MD). Participation was anonymous and voluntary. Participants were entered in a raffle to win a \$50 Visa gift card. The initial participation goal of 7,500 completed responses was met in 5 hours and 13,011 completed responses were collected ([MMCC 2023](#)).

FDA discussed the survey with MMCC investigators and requested summary data regarding the characteristics of survey participants, perceived effectiveness, and adverse events. These results were provided by MMCC investigators in tabular form. A description of the quality control process conducted by MMCC is described in the Appendix (*Cannabis Public Policy Consulting, Quality Control Processes*).

4.5.1.2. Maryland Results

All questions were optional in the survey; thus, the number of respondents varies by question. Descriptive characteristics of MMCC study participants are presented in Appendix [Table 66](#). Participants were mostly White or Caucasian (78.2%), female (53.8%), not Hispanic or Latino (93.7%), and employed full-time (56%); most had been in the medical cannabis program for less than 4 years (79.5%).

The frequencies of condition or symptom treated with cannabis are presented in [Table 50](#). The most frequently treated symptom was chronic pain (46%), other chronic condition (33.4%) and post-traumatic stress syndrome (12.5%).

Table 50. Most Common Condition or Symptom Treated With Cannabis Among Maryland Medical Cannabis Commission (MMCC) Survey Participants

Qualifying condition	n	%
Anorexia	131	1
Severe or persistent muscle spasms	387	3
Epileptic seizures	85	0.7
Severe or chronic pain	5980	46
Cachexia or wasting syndrome	20	0.2
Post-traumatic stress disorder (PTSD)	1622	12.5
Severe nausea	334	2.6
Other chronic condition	4343	33.4
Total	12902	

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Most participants reported using cannabis all or most days in the past month (65.1%). They used alcohol at least once in the past month (60%) and did not use other substances (Appendix [Table 67](#)). The primary methods of cannabis use were smoking, eating edibles, or vaping ([Table 50](#)). Additional information regarding the methods of consumption is provided in Appendix [Table 68](#).

Table 51. Primary Method of Marijuana Consumption in the Past Month, Maryland Medical Cannabis Commission (MMCC) Survey Participants

Method of Consumption	n	%
Smoking	6101	46.9
Ingesting edibles	2622	20.2
Vaping	2737	21
Dabbing, oil, wax, shatter, butter concentrate	467	3.6
Tinctures or oral sprays (elixirs)	178	1.4
Capsules or tablets	128	1
Topicals (balm, lotion, cream)	176	1.4
Transdermal (patch)	5	0
Rectal/Vaginal suppositories	10	0.1
Total	12424	

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Patients were asked if they used cannabis for recreational purposes; most patients used cannabis for medical use only (63.8%, [Table 52](#)). A small number of patients reported using cannabis for only (0.8%) or mostly recreational purposes (1.8%).

Table 52. Percentage of Medical Use vs. Recreational Use in the Past Month Among Maryland Medical Cannabis Commission (MMCC) Survey Participants

Percentage of Medical Use	n	%
100% medical	8298	63.8
75% med, 25% rec	2474	19
50% med, 50% rec	1547	11.9
25% med, 75% rec	231	1.8

Percentage of Medical Use	n	%
100% rec	100	0.8
Didn't use in past month	271	2.1
Total	12921	

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Most patients reported that they perceived cannabis treatment to be moderately (21.4%), very (46%), or extremely (28.3%) effective (Appendix [Table 69](#)). Patients were asked about the perceived health and social effects of cannabis treatment, most said it improved their physical (71.9%) and mental (88.6%) health as well as their social relationships (54.3%, Appendix [Table 70](#)). They reported cannabis either improved (37%) or had no impact (54.6%) on their memory or concentration.

Most patients reported never experiencing adverse events or symptoms while using cannabis (Appendix [Table 71](#) and [Table 72](#)). Over 80% reported never experiencing panic, psychotic or paranoid feelings, suicidal thoughts or ideation, breathing problems, and nausea/vomiting. The most common adverse condition experienced was anxiety, which was reported as experienced at least once among 31.1% of patients. There were very few patients who were treated in an emergency room or urgent care as a result of their cannabis use (< 2%, Appendix [Table 73](#)).

Patients were asked to report on a scale of 1= not interested at all to 10= very interested their degree of interest in reducing or cutting back cannabis consumption and most were not interested (Mean = 1.69, Standard Deviation =2.19).

Most medical cannabis users reported not driving within 3 hours of consuming cannabis or under the influence of cannabis (79.8%, Appendix [Table 74](#)).

4.5.1.3. Maryland Discussion

Overall patients using marijuana for medical purposes in MD reported very few side effects and a high level of perceived effectiveness. A strength of this study was the high participation rate. Additionally, since participation was anonymous and voluntary, patients were more likely to accurately report their experiences because there is no concern that they may lose access to marijuana based on their responses. However, participation was voluntary, thus generalizability may be limited.

There are several limitations of this study that should be considered. This was a cross-sectional study that only included patients currently enrolled in the program. Patients who were previously registered to use marijuana and experienced an adverse event or lack of perceived effectiveness were not included in this study, thus the number of adverse events may be underreported, and the perceived effectiveness may be overreported. Patients may also have been more motivated to report positive experiences with medical cannabis since the survey was conducted by the MMCC and patients would want to keep marijuana accessible in MD.

4.5.2. Minnesota

4.5.2.1. Minnesota Methods

Minnesota legalized the use of medical marijuana in 2014. The qualifying medical conditions for Minnesota (MN) are presented in [Appendix Table 75](#). Patients must complete a patient self-evaluation through the online MN medical cannabis patient registry before each medical cannabis purchase. For each adverse effect reported, patients were required to indicate the severity of that adverse effect as mild (symptoms do not interfere with daily activities), moderate (symptoms may interfere with daily activities), or severe (symptoms interrupt usual daily activities). MN provided summary data for 2015-2017 and raw data that were analyzed by two separate FDA analysts to ensure agreement from 2017-present.

4.5.2.2. Minnesota Results

Baseline characteristics of MN medical cannabis patients are presented in [Table 53](#). Most patients were white, and the primary qualifying conditions were chronic or intractable pain. A limitation of this study design is that patients who experienced an adverse event or did not perceive a benefit of marijuana likely would not make another marijuana purchase and these events would not be identified. To assess these potential differences in patient characteristics, FDA stratified baseline characteristics by the number of patient visits.

Table 53. Baseline Characteristics of Minnesota Medical Cannabis Patients 2017-2022*

Characteristic	Overall		Patients With at Least 1 Returning Visit		Patients Without a Returning Visit	
	n	%	n	%	n	%
Receive Medical Assistance	36606	50.04	16164	53.81	20442	47.41
Race/Ethnicity						
Hispanic	2760	3.77	1059	3.53	1701	3.94
American Indian	2881	3.94	1153	3.84	1728	4.01
Asian	1044	1.43	388	1.29	656	1.52
Black	5187	7.09	1693	5.64	3494	8.1
Unknown race	280	0.38	99	0.33	181	0.42
Hawaiian	204	0.28	67	0.22	137	0.32
No response for race	2845	3.89	1148	3.82	1697	3.94
Other race	1757	2.40	694	2.31	1063	2.47
White	61961	84.69	26057	86.74	35904	83.27
Certified Condition						
Cancer, where this illness or its treatment produces cachexia or severe wasting. Live July 1, 2015	1686	2.3	250	0.83	1436	3.33
Terminal illness, where this illness or its treatment produces severe or chronic pain. Live July 1, 2015	345	0.47	64	0.21	281	0.65
Terminal illness, where this illness or its treatment produces nausea or severe vomiting. Live July 1, 2015	220	0.3	40	0.13	180	0.42
Terminal illness, where this illness or its treatment produces cachexia or severe wasting. Live July 1, 2015	213	0.29	30	0.1	183	0.42
Glaucoma. Live July 1, 2015	403	0.55	185	0.62	218	0.51
HIV/AIDS. Live July 1, 2015	387	0.53	174	0.58	213	0.49
Tourette syndrome. Live July 1, 2015	313	0.43	149	0.5	164	0.38
Amyotrophic lateral sclerosis. Live July 1, 2015	130	0.18	36	0.12	94	0.22
Seizures, incl. those characteristic of epilepsy. Live July 1, 2015	1708	2.33	790	2.63	918	2.13
Severe and persistent muscle spasms, incl those characteristic of multiple sclerosis. Live July 1, 2015	5467	7.47	2997	9.98	2470	5.73
Inflammatory bowel disease, incl. Crohn's disease. Live July 1, 2015	1697	2.32	825	2.75	872	2.02
Intractable pain. Live August 1, 2016	31168	42.6	15668	52.16	15500	35.95
Post-traumatic stress disorder. Live August 1, 2017	20445	27.95	7991	26.6	12454	28.88
Autism. Live August 1, 2018	1421	1.94	664	2.21	757	1.76
Obstructive sleep apnea. Live August 1, 2018	2980	4.07	1526	5.08	1454	3.37

Alzheimer's disease. Live August 1, 2019	119	0.16	19	0.06	100	0.23
Chronic pain. Live August 1, 2020	24189	33.06	7310	24.34	16879	39.15
Sickle cell disease. Live August 1, 2021	14	0.02	2	0.01	12	0.03
Chronic vocal or motor tic disorder. Live August 1, 2021	70	0.1	10	0.03	60	

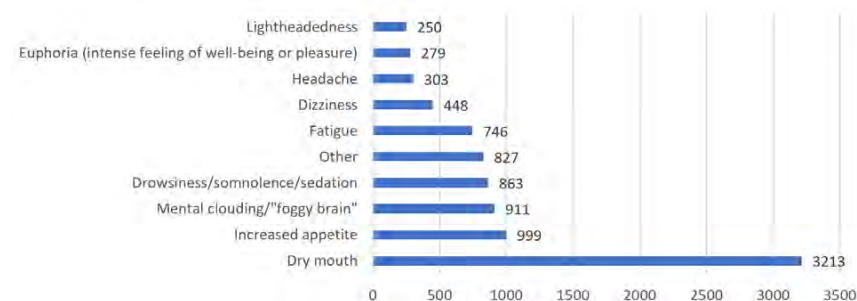
Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

Note:

- "Live" refers to when the certified condition was added to the patient survey
- When selecting race, patients can select more than one race
- Patients can be certified for multiple conditions at one time
- Patients must first be certified by a registered health care practitioner for at least one qualifying condition. After that certification is submitted, patients can enroll to be in the program. Enrollment is good for 1 year.

The most common side effects reported in 2021 are presented in [Figure 13](#), additional data regarding side effects are presented in Appendix [Table 76](#), [Table 77](#), and [Table 78](#). From 2017-2022, any side effect was reported in <10% of all patient surveys and less than 1% reported severe side effects (Appendix [Table 77](#)). The majority (>90%) of side effects reported by MN medical cannabis users were mild (symptoms do not interfere with daily activities) to moderate (symptoms may interfere with daily activities) in severity. The most common side effect reported was dry mouth; other side effects were increased appetite, somnolence, and mental clouding/foggy brain.

Figure 13. Top Ten Side Effects Reported on the MN Patient Self-Evaluation, 2021



Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

4.5.2.3. Minnesota Discussion

An advantage of the MN database is that all medical marijuana users are required to complete the patient survey before every purchase, thus these findings reflect the experience of medical marijuana patients in MN. However, patients may underreport side effects if they are concerned about the results of the survey being used to limit access to medical marijuana. Another limitation of the MN database is the lack of information from patients who chose to stop using medical marijuana. This could lead to an underestimation of the number of adverse events as well as an overestimation of perceived effectiveness and an underestimation of adverse events as patients who experienced adverse events or lack of effectiveness may not make a second purchase.

4.5.3. Conclusion

Chronic pain was the most common condition treated with marijuana. The side effects reported by marijuana patients in Minnesota were generally defined as mild (symptoms do not interfere with daily activities) by respondents. Most patients did not report any side effects in either Maryland or Minnesota. Patients in Maryland reported a high level of perceived effectiveness and symptom improvement because of their marijuana use. Survey participation was voluntary in Maryland, which may limit generalizability. Both the Maryland and Minnesota databases are limited because they did not include patients who stopped using marijuana, which may result in an overestimation of positive patient experiences.

4.6. Summary of FDA-Approved Drug Products Related to Marijuana

Although the focus of this document is on marijuana, CBD and Δ^9 -tetrahydrocannabinol (Δ^9 -THC) are the two major phytocannabinoids present in the *Cannabis sativa* plant, and there are several FDA approved products that contain botanical, synthetic, or structurally related forms of these components of marijuana. The following sections summarize FDA's findings for these products as reflected in their approved labeling, and, although these products do not fall under the definition of marijuana, the findings for these products are relevant to the discussion of the medical use of marijuana.

Marinol (Dronabinol) Capsules, for Oral Use, Approved by FDA in 1985

Marinol capsules, a Schedule III controlled substance, contains synthetically derived Δ^9 -THC (the (-)-trans stereoisomer, also known as dronabinol) that is approved for the treatment of anorexia associated with weight loss in patients with AIDS and nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Marinol is supplied as capsules in strengths of 2.5 mg, 5 mg, and 10 mg.

Marinol has identical warnings and precautions, as well as common adverse events, to Syndros.

Syndros (Dronabinol) Oral Solution, Approved by FDA in 2016

Syndros oral solution, a Schedule II controlled substance, contains synthetically-derived Δ^9 -THC (dronabinol) that is approved for the treatment of anorexia associated with weight loss in patients with AIDS and nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Syndros is supplied as a 5 mg/ml solution.

Syndros has warnings and precautions within the labeling describing neuropsychiatric effects, hemodynamic effects, seizures, substance use, and paradoxical nausea/vomiting, as well as drug interactions. The most common adverse reactions ($\geq 3\%$) are abdominal pain, dizziness, euphoria, nausea, paranoid reaction, somnolence, thinking abnormal, and vomiting.

Cesamet (Nabilone) Capsules, Approved by FDA in 1985

Nabilone, the active ingredient in Cesamet capsules, is a Schedule II controlled substance that is a synthetic analogue of Δ^9 -THC. Cesamet is approved for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Cesamet is supplied as 1 mg capsules.

Cesamet has similar safety information to other synthetic forms of Δ^9 -THC.

Epidiolex (Cannabidiol) Oral Solution, Approved by FDA in 2018

Epidiolex oral solution is not a controlled substance and is a highly purified form of cannabidiol approved for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients 1 year of age and older.

Epidiolex is considered to have no meaningful potential for abuse.

FDA included a review of approved products relevant to marijuana because the active pharmaceutical ingredients (APIs) in the approved products, such as synthetic forms of THC, are

expected to have the same clinical effect as botanically-derived THC. Therefore, if the above approved formulations of THC were considered to have proven benefit for various indications, it is logical to conclude that a similar dose administered through a marijuana preparation would be relevant to informing potential therapeutic uses of marijuana for drug scheduling purposes.

4.7. Summary of Expert Opinions and Position Statements

Summary of Professional Organizations' Positions

[Table 54](#) provides a summary of a representative list of professional organizations' position statements on marijuana as it relates to their respective medical specialty. Most of these organizations did not arrive at a firm recommendation for use of marijuana in their specialty, but some acknowledged there may be preliminary evidence showing marijuana may have some therapeutic benefits. Otherwise, the majority of organizations acknowledged patient reported benefits and some evidence from clinical studies for cannabis-based treatments in their respective specialties, though they recommended more extensive research into cannabis rather than a recommendation to prescribe it for a particular disorder. Additionally, a number of organizations recommended rescheduling of cannabis from Schedule I to Schedule II to facilitate less barriers to quality research.

Table 54. Professional Organizations' Position Statements

Professional Organization	Highlights
American Academy of Family Physicians (2019) (AAFP 2019)	<ul style="list-style-type: none"> • "AAFP acknowledges preliminary evidence indicates marijuana and cannabinoids may have potential therapeutic benefits, while also recognizing subsequent negative public health and health outcomes associated with cannabis use." • Opposes the recreational use of marijuana. However, the AAFP supports decriminalization of possession of marijuana for personal use. • "The AAFP calls for decreased regulatory barriers to facilitate clinical and public health cannabis research, including reclassifying cannabis from a Schedule I controlled substance."
American Academy of Neurology (2020) (AAN 2020)	<ul style="list-style-type: none"> • Does not support the use of, nor any assertion of therapeutic benefits of, cannabis products as medicines for neurologic disorders in the absence of sufficient scientific peer-reviewed research to determine their safety and specific efficacy • Supports efforts to allow rigorous research to evaluate long term safety and efficacy
American Epilepsy Society (2022) (AES 2022)	<ul style="list-style-type: none"> • Scientific evidence for the use of cannabis itself in the treatment of epilepsy is highly limited • Calls for increased rigorous clinical research, AES urges that the status of cannabis as a United States Drug Enforcement Administration (DEA) Schedule I controlled substance be reviewed. • The AES call for rescheduling is not an endorsement of the legalization of cannabis but rather is a recognition that the current restrictions on the use of cannabis products for research continue to significantly limit scientifically rigorous research
American Psychiatric Association (2019) (APA 2018)	<ul style="list-style-type: none"> • Does not endorse cannabis as medicine • Association with onset of psychiatric disorders

Professional Organization	Highlights
American Society of Addiction Medicine (2020) (ASAM 2020)	<ul style="list-style-type: none"> • "Cannabis used for medical purposes should be rescheduled from Schedule I of the Controlled Substances Act (CSA) to promote more clinical research and FDA oversight typical of other medications." • Position paper summarized risks and benefits but did not state whether they agreed with findings on efficacy. • Healthcare professionals should only recommend non-FDA-approved cannabis if there is evidence that the potential benefits outweigh the potential harms.
The Association for Addiction Professionals (NAADAC) (NAADAC 2022)	<ul style="list-style-type: none"> • Does not currently support the use of cannabis as medicine or for recreational purposes • Acknowledges some early evidence of efficacy and encourages further research
International Association for the Study of Pain (2021) (IASP 2021)	<ul style="list-style-type: none"> • The IASP found a lack of high-quality evidence • The evidence base regarding efficacy and safety fails to reach the threshold at which IASP can endorse their general use for pain control • Acknowledge patient experience can show benefit and call for more rigorous and robust research
American Academy of Sleep Medicine Position Statement (Ramar et al. 2018)	<ul style="list-style-type: none"> • Limited evidence citing small pilot or proof of concept studies suggest that the synthetic medical cannabis extract dronabinol may improve respiratory stability and provide benefit to treat obstructive sleep apnea (OSA). • "It is the position of the American Academy of Sleep Medicine (AASM) that medical cannabis and/or its synthetic extracts should not be used for the treatment of OSA due to unreliable delivery methods and insufficient evidence of effectiveness, tolerability, and safety." • Further research recommended

5. Overall Conclusions for Part 2 of the Currently Accepted Medical Use Test for Marijuana

Based on the totality of the available data described in Section [II.4](#) of this document, we conclude that there exists some credible scientific support for the use of marijuana in at least one of the indications for which there is widespread current experience with its medical use in the United States, as identified under Part 1 of the CAMU test. The analysis and conclusions on the available data are not meant to imply that safety and efficacy have been established for marijuana that would support FDA approval of marijuana for any particular indication. However, the available data do provide some level of substantiation to support the way marijuana is evidently being used in clinical practice.

As previously noted, in evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors considered in favor of a positive finding included whether 1) favorable clinical studies, although not necessarily FDA approval-level studies, of the medical use of marijuana have been published in peer-reviewed journals and/or 2) qualified expert organizations (e.g., academic or professional societies, government agencies) have opined in favor of the medical use or provided guidance to practitioners on the medical use. Factors considered that weigh against a finding that Part 2 of the CAMU test is met

included whether 1) data or information indicate that medical use of the substance is associated with unacceptably high safety risks for the likely patient population, e.g., due to toxicity concerns; 2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; and/or 3) qualified expert organizations (e.g., academic or professional societies, government agencies) have recommended against the medical use of marijuana.

Our analysis of the available information showed mixed findings across indications. The largest evidence base substantiating the use of marijuana in clinical practice exists for its use in treating pain (in particular, neuropathic pain). In the pain indication, the UF analysis found inconclusive results; however, numerous other systematic reviews concluded that there exists some level of evidence supporting the use of marijuana for pain. UF found that there is low to moderate quality evidence supporting the effectiveness of marijuana as medical treatment for outcomes in anorexia related to certain medical conditions, nausea and vomiting, and PTSD; however, FDA review of systematic reviews showed mixed results, mostly in support of synthetic forms or evidence only in observational studies with high risk of bias, which are not relevant to this discussion. In particular, FDA found that the potential for psychiatric adverse events associated with treating PTSD with marijuana may be more substantial than any limited benefit in observational studies. Although UF did not conclude that there was evidence in support of the efficacy/effectiveness of marijuana in IBD, both their review and other systematic reviews found some benefit with respect to subjective symptoms in this condition. With regard to epilepsy and anxiety, both UF's review and FDA's review of systematic reviews did not find support for the benefit of marijuana in the treatment of these conditions. Where positive, the effects of marijuana use and the quality of evidence were generally in the low to moderate range. UF did not find high quality evidence supporting worsening of outcomes in any indication.

None of the evidence from the systematic reviews included in our analysis demonstrated substantial safety concerns that would argue against the use of marijuana in any of the indications where there exists some support for its benefit. However, generally, data on safety from both clinical trials and observational studies were sparse. Literature shows marijuana has more adverse events when compared to a placebo or active control group, however, typically in the mild to moderate range. Severe adverse events were uncommon. Surveys of patients using marijuana in Maryland and Minnesota found most patients did not report any side effects and those that did report side effects mostly described them as mild. Neither of the state databases included patients who chose to stop using marijuana, which may result in an overestimation of positive experiences and an underestimation of adverse events. To date, observational data sources available to FDA, in general, lack the necessary elements to identify the exposure, to distinguish the reason for use (medical vs. recreational) and the condition that prompted its medical use, and/or to permit sound inferential analyses. Data from U.S. national surveys, although, overall, lacking sufficient details on patient's characteristics and factors that prompted the use of marijuana for medical purposes, and impacted by the COVID-19 pandemic, suggested that medical use of marijuana increases as age increases. Only data from one survey provided information on intended indication for use, suggesting that users often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms, but approximately only half of them reportedly had ever asked a healthcare professional for a recommendation to use medical marijuana.

Although the safety data obtained from use in a medical context are considered to be the most relevant for the CAMU Part 2 analysis, FDA evaluated the safety of marijuana in the nonmedical setting to inform the potential for more severe outcomes. Specifically, FDA evaluated safety outcomes related to the nonmedical use of, use of uncertain intent of, and unintentional exposure to marijuana through a variety of epidemiological data sources, including the National Poison Data System (NPDS), Drug-Involved Mortality (DIM), National Vital Statistics System-Mortality (NVSS-M), National Emergency Department Sample (NEDS), National Inpatient Sample (NIS), FDA's Sentinel, FDA Adverse Event Reporting System/Center for Food Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (FAERS/CAERS), Medicare, ToxIC Core Registry, and Drug Abuse Warning Network (DAWN). Safety outcomes for marijuana were evaluated relative to several comparator substances controlled under the CSA, including drugs in Schedule I: heroin (an illicit opioid drug); Schedule II: hydrocodone and oxycodone (approved opioid prescription drugs), cocaine and fentanyl (largely illicitly produced drugs in the nonmedical use setting, although there are approved prescription drugs); Schedule III: ketamine (an approved prescription drug); and Schedule IV: zolpidem, benzodiazepines, and tramadol (approved prescription drugs). The comparative data demonstrate that, although marijuana is frequently used nonmedically, marijuana has a less concerning overall safety profile relative to the comparators for a number of important outcomes (e.g., single substance use overdose death, hospitalizations). However, in young children, population-adjusted rates of emergency department visits and hospitalizations involving marijuana poisoning were higher than heroin, cocaine, and benzodiazepines for the periods studied. Of note, some of the comparator substances are approved for use in conditions similar to the indications for which marijuana is being evaluated in this CAMU analysis (e.g., opioids for pain, benzodiazepines for anxiety-related conditions) (FDA, *Office of Surveillance and Epidemiology*, 2023).

We also considered position statements from professional organizations relevant to the indications discussed. The vast majority of professional organizations did not recommend the use of marijuana in their respective specialty; however, none specifically recommended against it, with the exception of the APA, who stated that marijuana is known to worsen certain psychiatric conditions.

On balance, the available data indicate that there is some credible scientific support to substantiate the use of marijuana in the treatment of: pain; anorexia related to certain medical conditions; and nausea and vomiting (e.g. chemotherapy-induced), with varying degrees of support and consistency of findings.

III. Appendix

4. International Country Policy Study (ICPS)

Country	ICPS Score	ICPS Rating
Algeria	1.0	Low
Angola	1.0	Low
Argentina	2.0	Low
Armenia	2.0	Low
Australia	3.0	Low
Austria	3.0	Low
Azerbaijan	1.0	Low
Bahrain	3.0	Low
Bangladesh	1.0	Low
Barbados	3.0	Low
Belarus	1.0	Low
Belgium	3.0	Low
Belize	3.0	Low
Benin	1.0	Low
Bhutan	1.0	Low
Bolivia	1.0	Low
Bosnia and Herzegovina	1.0	Low
Brazil	2.0	Low
Bulgaria	2.0	Low
Burkina Faso	1.0	Low
Burundi	1.0	Low
Cambodia	1.0	Low
Cameroon	1.0	Low
Canada	3.0	Low
Cape Verde	3.0	Low
Casakhstan	1.0	Low
Cayman Islands	3.0	Low
Czech Republic	3.0	Low
Dominican Republic	3.0	Low
Dominica	3.0	Low
DRC	1.0	Low
Ecuador	2.0	Low
Egypt	1.0	Low
El Salvador	1.0	Low
Equatorial Guinea	1.0	Low
Estonia	3.0	Low
Ethiopia	1.0	Low
Fiji	3.0	Low
Finland	3.0	Low
France	3.0	Low
Gabon	1.0	Low
Gambia	1.0	Low
Germany	3.0	Low
Ghana	1.0	Low
Greece	3.0	Low
Guatemala	1.0	Low
Honduras	1.0	Low
Hong Kong	3.0	Low
Hungary	2.0	Low
India	1.0	Low
Indonesia	1.0	Low
Iran	1.0	Low
Ireland	3.0	Low
Israel	2.0	Low
Italy	3.0	Low
Jamaica	3.0	Low
Japan	3.0	Low
Jordan	1.0	Low
Kazakhstan	1.0	Low
Kenya	1.0	Low
Korea	3.0	Low
Kuwait	3.0	Low
Latvia	3.0	Low
Lebanon	1.0	Low
Lesotho	1.0	Low
Lithuania	3.0	Low
Luxembourg	3.0	Low
Macao	3.0	Low
Madagascar	1.0	Low
Mali	1.0	Low
Maldives	1.0	Low
Mexico	2.0	Low
Moldova	1.0	Low
Morocco	1.0	Low
Mozambique	1.0	Low
Netherlands	3.0	Low
Nicaragua	1.0	Low
Niger	1.0	Low
Nigeria	1.0	Low
North Macedonia	1.0	Low
Norway	3.0	Low
Oman	3.0	Low
Pakistan	1.0	Low
Panama	3.0	Low
Papua New Guinea	1.0	Low
Paraguay	2.0	Low
Peru	2.0	Low
Philippines	1.0	Low
Poland	3.0	Low
Portugal	3.0	Low
Romania	2.0	Low
Russia	1.0	Low
Rwanda	1.0	Low
Saudi Arabia	3.0	Low
Senegal	1.0	Low
Serbia	1.0	Low
Seychelles	3.0	Low
Singapore	3.0	Low
Slovakia	3.0	Low
Slovenia	3.0	Low
South Africa	2.0	Low
South Korea	3.0	Low
Spain	3.0	Low
Sri Lanka	1.0	Low
Sweden	3.0	Low
Switzerland	3.0	Low
Taiwan	3.0	Low
Tanzania	1.0	Low
Togo	1.0	Low
Tonga	3.0	Low
Turkey	2.0	Low
Turkmenistan	1.0	Low
Uganda	1.0	Low
Ukraine	1.0	Low
United Arab Emirates	3.0	Low
United Kingdom	3.0	Low
United States	3.0	Low
Uruguay	3.0	Low
Uzbekistan	1.0	Low
Venezuela	1.0	Low
Vietnam	1.0	Low
Yemen	1.0	Low
Zambia	1.0	Low
Zimbabwe	1.0	Low

Table 56. Sample Characteristics, ICPS, 2018-2021

Characteristic	Wave 1 - 2018 (n=17,112)	Wave 2 - 2019 (n=30,479)	Wave 3 - 2020 (n=29,900)	Wave 4 - 2021 (n=30,081)
Sex				
Female	50.2% (8,586)	50.2% (15,290)	50.1% (14,995)	50.1% (15,080)
Male	49.8% (8,526)	49.8% (15,189)	49.9% (14,905)	49.9% (15,001)
Age (NSDUH)				
16-17	14.1% (2,358)	8.1% (2,432)	7.1% (2,062)	6.7% (1,954)
18-25	6.2% (1,042)	12.1% (3,619)	13.8% (4,027)	13.8% (4,056)
26-44	19.6% (3,270)	19.8% (5,924)	18.6% (5,437)	19.0% (5,576)
45-64	60.1% (10,054)	59.9% (17,914)	60.5% (17,645)	60.5% (17,757)
Race				
White	76.4% (13,068)	76.0% (23,158)	75.8% (22,655)	75.6% (22,730)
Black/African American	13.6% (2,335)	13.8% (4,201)	13.9% (4,148)	13.9% (4,183)
Asian	3.8% (648)	4.0% (1,207)	4.6% (1,368)	3.8% (1,132)
American Indian or Alaskan Native	0.8% (140)	1.3% (383)	1.0% (288)	1.1% (324)
Native Hawaiian or Pacific Islander	0.2% (34)	0.3% (105)	0.4% (110)	0.4% (129)
Other	5.2% (887)	4.7% (1,424)	4.5% (1,331)	5.3% (1,583)
Ethnicity				
Hispanic	8.8% (1,493)	12.6% (3,788)	11.5% (3,391)	13.7% (4,063)
Non-Hispanic	91.2% (15,507)	87.4% (26,355)	88.5% (26,086)	86.3% (25,616)
Education				
< High school	14.5% (2,470)	10.4% (3,146)	9.8% (2,900)	10.4% (3,106)
High school	18.7% (3,192)	22.0% (6,688)	23.2% (6,889)	22.7% (6,783)
Some college	39.2% (6,691)	37.8% (11,481)	36.9% (10,946)	36.6% (10,922)
Bachelor's degree	27.6% (4,702)	29.8% (9,039)	30.1% (8,916)	30.2% (9,012)
Income Adequacy				
Very difficult/Difficult	31.3% (5,268)	34.1% (10,213)	27.7% (8,090)	29.7% (8,677)
Neither easy nor difficult	32.2% (5,421)	33.6% (10,075)	35.7% (10,416)	33.6% (9,824)
Easy/Very easy	35.8% (6,029)	31.1% (9,335)	35.1% (10,226)	35.1% (10,266)
Not reported	0.8% (137)	1.2% (350)	1.5% (425)	1.6% (458)
Jurisdiction				
'Illegal' states	22.7% (3,890)	13.9% (4,230)	18.2% (5,437)	16.6% (4,980)
'Medical' states	34.0% (5,824)	19.8% (6,045)	23.6% (7,071)	17.2% (5,160)
'Recreational' states	43.2% (7,398)	66.3% (20,204)	58.2% (17,392)	66.3% (19,941)

Characteristic	Wave 1 - 2018 (n=17,112)	Wave 2 - 2019 (n=36,479)	Wave 3 - 2020 (n=29,900)	Wave 4 - 2021 (n=30,001)
Frequency of Use				
Ever consumer	53.0% (5,150)	49.0% (9,563)	50.1% (8,809)	46.7% (9,001)
Past 12-month consumer (monthly)	13.3% (1,280)	13.5% (2,627)	12.0% (2,113)	12.7% (2,448)
Monthly consumer	9.9% (951)	9.6% (1,876)	9.5% (1,675)	10.3% (1,992)
Weekly consumer	8.4% (809)	8.0% (1,555)	8.3% (1,451)	8.9% (1,718)
Daily consumer ^a	14.7% (1,413)	20.0% (3,907)	20.1% (3,511)	21.4% (4,122)

Source: [Canadian Institute for Public and Social Affairs \(CIPSA\) Table 1](#)
Footnote: ^aConsumption of at least one pack per week.
Abbreviations: CIPSA, International Cannabis Policy Study; NSDUH, National Survey on Drug Use and Health

Table 57. Time Since Last Cannabis Use Among Exclusive Past-Year Medical Cannabis Consumers, Recency of Use by Sex, ICPS, 2021

Time Since Last Use ¹	Male (n=780)	Female (n=667)	Overall (n=1,447)
All States			
Past 12-months	36.2% (282) (30.4% - 42.0%)	29.0% (194) (24.7% - 33.4%)	32.9% (476) (29.2% - 36.6%)
Past month	63.8% (498) (58.0% - 69.6%)	71.0% (473) (66.6% - 75.3%)	67.1% (971) (63.4% - 70.8%)
'Illegal' States			
Past 12-months	44.0% (81) (30.1% - 57.9%)	37.7% (63) (28.7% - 46.7%)	41.0% (144) (32.5% - 49.5%)
Past month	56.0% (103) (42.1% - 69.9%)	62.3% (104) (53.3% - 71.3%)	59.0% (207) (50.5% - 67.5%)
'Medical' States			
Past 12-months	37.7% (93) (27.2% - 48.3%)	21.7% (44) (15.4% - 28.0%)	30.6% (138) (24.0% - 37.2%)
Past month	62.3% (155) (51.7% - 72.8%)	78.3% (157) (72.0% - 84.6%)	69.4% (312) (62.8% - 76.0%)
'Recreational' States			
Past 12-months	31.0% (108) (23.7% - 38.2%)	29.1% (87) (22.0% - 36.1%)	30.1% (194) (25.0% - 35.2%)
Past month	69.0% (240) (61.8% - 76.3%)	70.9% (212) (63.9% - 78.0%)	69.9% (452) (64.8% - 75.0%)

Source: (Hammond et al. 2023), Table 57.

¹ The categories 'Past 12-months' and 'Past month' are mutually exclusive.**Table 58. Time Since Last Cannabis Use Among Exclusive Past Year Medical Cannabis Consumers, Recency of Use by Age (NSDUH Age Categories), ICPS, 2021**

Time Since Last Use ^{1,2,3}	16-17 (n=37)	18-25 (n=180)	26-34 (n=327)	35-64 (n=891)	Overall (n=1,435)
All States					
Past 12-months	33.0% (12) (10.5% - 55.5%)	30.7% (55) (20.8% - 40.6%)	32.2% (105) (23.4% - 41.1%)	33.7% (300) (29.1% - 38.2%)	33.0% (473) (29.2% - 36.7%)
Past month	67.0% (25) (44.5% - 89.5%)	69.3% (125) (59.4% - 79.2%)	67.8% (222) (58.9% - 76.6%)	66.3% (591) (61.8% - 70.9%)	67.0% (962) (63.3% - 70.8%)

Time Since Last Use^{1,2,3}	16-17 (n=37)	18-25 (n=180)	26-34 (n=327)	35-64 (n=891)	Overall (n=1,435)
'Illegal' States					
Past 12-months	19.7% (3) (0.0% - 46.4%)	30.3% (17) (11.5% - 49.2%)	64.3% (44) (42.8% - 85.9%)	38.2% (80) (28.4% - 48.0%)	41.3% (144) (32.7% - 49.8%)
Past month	80.3% (12) (53.6% - 100.0%)	69.7% (39) (50.8% - 88.5%)	35.7% (24) (14.1% - 57.2%)	61.8% (130) (52.0% - 71.6%)	58.7% (205) (50.2% - 67.3%)
'Medical' States					
Past 12-months	58.4% (4) (9.2% - 100.0%)	38.8% (18) (15.9% - 61.7%)	26.1% (31) (12.3% - 39.9%)	30.1% (82) (22.1% - 38.0%)	30.4% (135) (23.8% - 37.1%)
Past month	41.6% (3) (0.0% - 90.8%)	61.2% (29) (38.3% - 84.1%)	73.9% (86) (60.1% - 87.7%)	69.9% (191) (62.0% - 77.9%)	69.6% (309) (62.9% - 76.2%)
'Recreational' States					
Past 12-months	32.8% (5) (0.0% - 68.2%)	26.0% (20) (14.3% - 37.7%)	21.8% (31) (13.3% - 30.4%)	33.8% (138) (27.0% - 40.5%)	30.2% (194) (25.1% - 35.3%)
Past month	67.2% (10) (31.8% - 100.0%)	74.0% (57) (62.3% - 85.7%)	78.2% (111) (69.6% - 86.7%)	66.2% (270) (59.5% - 73.0%)	69.8% (448) (64.7% - 74.9%)

Source: (Hammond et al. 2023), Table 51.

¹ The categories 'Past 12-months' and 'Past month' are mutually exclusive.² 12 responses were excluded.³ In some cases, the sum of the weighted frequencies for state categories does not equal the total frequency as a result of rounding.

Abbreviations: ICPS, International Cannabis Policy Study; NSDUH, National Survey on Drug Use and Health

Table 59. Time Since Last Cannabis Use Among Exclusive Past-Year Medical Cannabis Consumers, Recency of Use by Race, ICPS, 2021

Time Since Last Use^{1,2}	American Indian or Alaskan Native (n=25)	Asian (n=18)	Black or African American (n=227)	Native Hawaiian or Pacific Islander (n=8)	White (n=1,086)	Other (n=83)	Overall (n=1,447)
All States							
Past 12-months	18.6% (5) (3.0% - 34.2%)	45.6% (8) (8.9% - 82.3%)	41.2% (94) (29.8% - 52.7%)	56.0% (4) (0.2% - 100.0%)	32.1% (348) (28.0% - 36.2%)	20.0% (17) (8.6% - 31.4%)	32.9% (476) (29.2% - 36.6%)
Past month	81.4% (20) (65.8% - 97.0%)	54.4% (10) (17.7% - 91.1%)	58.8% (133) (47.3% - 70.2%)	44.0% (3) (0.0% - 99.8%)	67.9% (737) (63.8% - 72.0%)	80.0% (67) (68.6% - 91.4%)	67.1% (971) (63.4% - 70.8%)
'Illegal' States							
Past 12-months	0.0% (0) (0.0% - 0.0%)	76.4% (2) (25.9% - 100.0%)	52.2% (52) (33.0% - 71.4%)	0.0% (0) (0.0% - 0.0%)	36.4% (84) (27.2% - 45.6%)	41.4% (6) (7.2% - 75.6%)	41.0% (144) (32.5% - 49.5%)
Past month	100.0% (4) (100.0% - 100.0%)	23.6% (0)* (0.0% - 74.1%)	47.8% (48) (28.6% - 67.0%)	0.0% (0) (0.0% - 0.0%)	63.6% (146) (54.4% - 72.8%)	58.6% (9) (24.4% - 92.8%)	59.0% (207) (50.5% - 67.5%)

Time Since Last Use ^{1,2}	American Indian or Alaskan Native (n=25)	Asian (n=18)	Black or African American (n=227)	Native Hawaiian or Pacific Islander (n=8)	White (n=1,086)	Other (n=83)	Overall (n=1,447)
‘Medical’ States							
Past 12-months	25.8% (1) (0.0% - 69.5%)	0.0% (0) (0.0% - 0.0%)	39.3% (21) (15.7% - 62.8%)	0.0% (0) (0.0% - 0.0%)	29.9% (109) (22.8% - 37.1%)	25.9% (6) (1.9% - 49.9%)	30.6% (138) (24.0% - 37.2%)
Past month	74.2% (4) (30.5% - 100.0%)	100.0% (3) (100.0% - 100.0%)	60.7% (33) (37.2% - 84.3%)	100.0% (1) (100.0% - 100.0%)	70.1% (255) (62.9% - 77.2%)	74.1% (17) (50.1% - 98.1%)	69.4% (312) (62.8% - 76.0%)
‘Recreational’ States							
Past 12-months	20.7% (3) (0.5% - 40.8%)	49.3% (7) (3.2% - 95.5%)	27.5% (20) (14.7% - 40.3%)	66.4% (4) (11.3% - 100.0%)	31.6% (156) (25.7% - 37.5%)	10.2% (5) (0.7% - 19.7%)	30.1% (194) (25.0% - 35.2%)
Past month	79.3% (12) (59.2% - 99.5%)	50.7% (7) (4.5% - 96.8%)	72.5% (52) (59.7% - 85.3%)	33.6% (2) (0.0% - 88.7%)	68.4% (336) (62.5% - 74.3%)	89.8% (41) (80.3% - 99.3%)	69.9% (452) (64.8% - 75.0%)

Source: (Hammond et al., 2023), Table 53.

* Weighted frequency rounded down to 0.

¹ The categories ‘Past 12-months’ and ‘Past month’ are mutually exclusive² In some cases, the sum of the weighted frequencies for state categories does not equal the total frequency as a result of rounding.**Table 60. Time Since Last Cannabis Use Among Exclusive Past-Year Medical Cannabis Consumers, Recency of Use by Ethnicity, ICPS, 2021**

Time Since Last Use ^{1,2}	Hispanic (n=274)	Non-Hispanic (n=1,158)	Overall (n=1,432)
All States			
Past 12-months	31.7% (87) (23.0% - 40.4%)	32.9% (380) (28.7% - 37.0%)	32.6% (467) (28.9% - 36.4%)
Past month	68.3% (187) (59.6% - 77.0%)	67.1% (778) (63.0% - 71.3%)	67.4% (965) (63.6% - 71.1%)
‘Illegal’ States			
Past 12-months	29.6% (13) (10.1% - 49.2%)	42.3% (128) (33.0% - 51.6%)	40.7% (141) (32.1% - 49.2%)
Past month	70.4% (31) (50.8% - 89.9%)	57.7% (175) (48.4% - 67.0%)	59.3% (206) (50.8% - 67.9%)
‘Medical’ States			
Past 12-months	18.2% (12) (5.3% - 31.2%)	32.2% (122) (25.0% - 39.5%)	30.2% (134) (23.6% - 36.8%)
Past month	81.8% (52) (68.8% - 94.7%)	67.8% (257) (60.5% - 75.0%)	69.8% (309) (63.2% - 76.4%)

Time Since Last Use ^{1,2}	Hispanic (n=274)	Non-Hispanic (n=1,158)	Overall (n=1,432)
'Recreational' States			
Past 12-months	37.4% (62) (25.1% - 49.8%)	27.4% (130) (22.0% - 32.7%)	30.0% (192) (24.9% - 35.1%)
Past month	62.6% (104) (50.2% - 74.9%)	72.6% (346) (67.3% - 78.0%)	70.0% (450) (64.9% - 75.1%)

Source: (Hammond et al. 2023), Table 55.

¹ The categories 'Past 12-months' and 'Past month' are mutually exclusive.

² 15 responses were excluded.

Table 61. Time Since Last Cannabis Use Among Exclusive Past-Year Medical Cannabis Consumers, Recency of Use by Cannabis Source, ICPS, 2021

Source ^{1,2}	Made/ Grown by Self	Family/ Friend	Dealer	Internet/ Mail Order	Store/ Dispensary	Other	Unknown
All States							
Past 12-months (n=476)	19.9% (95) (14.3% - 25.6%)	48.4% (230) (41.5% - 55.4%)	34.7% (165) (27.8% - 41.6%)	20.8% (99) (14.6% - 26.9%)	34.8% (166) (28.3% - 41.4%)	0.1% (0*) (0.0% - 0.3%)	1.2% (6) (0.0% - 2.5%)
Past month (n=971)	17.9% (174) (13.9% - 21.8%)	42.8% (416) (38.2% - 47.5%)	30.1% (293) (25.8% - 34.4%)	16.8% (164) (12.6% - 21.1%)	57.0% (553) (52.2% - 61.7%)	0.6% (6) (0.0% - 1.3%)	1.1% (10) (0.3% - 1.8%)
Overall (n=1,447)	18.6% (268) (15.3% - 21.8%)	44.7% (646) (40.8% - 48.6%)	31.6% (458) (28.0% - 35.3%)	18.1% (262) (14.7% - 21.6%)	49.7% (719) (45.8% - 53.6%)	0.5% (7) (0.0% - 0.9%)	1.1% (16) (0.5% - 1.8%)
'Illegal' States							
Past 12-months	24.1% (35) (10.9% - 37.3%)	45.3% (65) (31.1% - 59.6%)	46.4% (67) (31.8% - 61.1%)	21.9% (32) (8.6% - 35.3%)	33.3% (48) (19.3% - 47.2%)	0.0% (0) (0.0% - 0.0%)	0.0% (0) (0.0% - 0.0%)
Past month	15.6% (32) (7.3% - 23.8%)	56.2% (116) (46.0% - 66.5%)	41.1% (85) (30.9% - 51.4%)	14.4% (30) (7.4% - 21.4%)	37.3% (77) (27.4% - 47.1%)	0.0% (0) (0.0% - 0.0%)	0.2% (0*) (0.0% - 0.7%)
Overall	19.1% (67) (11.8% - 26.4%)	51.8% (182) (43.3% - 60.2%)	43.3% (152) (34.8% - 51.8%)	17.5% (61) (10.6% - 24.4%)	35.6% (125) (27.6% - 43.7%)	0.0% (0) (0.0% - 0.0%)	0.1% (0*) (0.0% - 0.4%)
'Medical' States							
Past 12-months	20.9% (29) (9.4% - 32.5%)	51.6% (71) (38.1% - 65.2%)	29.4% (40) (16.8% - 42.0%)	19.6% (27) (8.3% - 30.9%)	24.0% (33) (13.2% - 34.8%)	0.0% (0) (0.0% - 0.0%)	2.9% (4) (0.0% - 7.1%)
Past month	19.2% (60) (12.2% - 26.3%)	38.7% (121) (31.0% - 46.4%)	29.7% (93) (22.5% - 36.8%)	7.1% (22) (3.4% - 10.8%)	58.0% (181) (50.0% - 66.1%)	0.4% (1) (0.0% - 1.3%)	1.9% (6) (0.0% - 3.8%)
Overall	19.7% (89) (13.8% - 25.7%)	42.6% (192) (35.9% - 49.4%)	29.6% (133) (23.3% - 35.8%)	10.9% (49) (6.5% - 15.3%)	47.6% (214) (40.7% - 54.5%)	0.3% (1) (0.0% - 0.9%)	2.2% (10) (0.4% - 4.0%)

Source ^{1,2}	Made/ Grown by Self	Family/ Friend	Dealer	Internet/ Mail Order	Store/ Dispensary	Other	Unknown
‘Recreational’ States							
Past 12- months	16.1% (31) (10.7% - 21.6%)	48.4% (94) (38.7% - 58.2%)	29.9% (58) (21.3% - 38.5%)	20.7% (40) (12.5% - 29.0%)	43.7% (85) (34.0% - 53.3%)	0.2% (0*) (0.0% - 0.7%)	0.9% (2) (0.0% - 2.0%)
Past month	18.0% (81) (12.0% - 23.9%)	39.6% (179) (32.7% - 46.5%)	25.4% (115) (19.3% - 31.5%)	24.7% (112) (17.2% - 32.3%)	65.3% (295) (58.4% - 72.1%)	1.1% (5) (0.0% - 2.3%)	0.9% (4) (0.0% - 1.8%)
Overall	17.4% (113) (13.0% - 21.9%)	42.2% (273) (36.6% - 47.9%)	26.8% (173) (21.8% - 31.8%)	23.5% (152) (17.6% - 29.4%)	58.8% (380) (53.1% - 64.5%)	0.8% (5) (0.0% - 1.7%)	0.9% (6) (0.2% - 1.6%)

Source: (Hammann et al., 2023), Table 59.

* Weighted frequency rounded down to 0.

¹ Response options are not mutually exclusive, row totals may sum to greater than 100%.² The categories ‘Past 12-months’ and ‘Past month’ are mutually exclusive.**Table 62. Cannabis Purchasing by Type of Store Among Exclusive Past-Year Medical Cannabis Consumers Who Bought Cannabis From a Store, 2021**

Store ^{1,2,3,4}	Legal Medical Dispensary	Legal Recreational Store	An Illegal/ Unauthorized Store	Other Type of Store/ Dispensary
All States				
Past 12-months (n=164)	69.9% (115) (59.8% - 80.1%)	41.2% (67) (29.7% - 52.6%)	10.1% (16) (3.6% - 16.6%)	1.3% (2) (0.0% - 2.8%)
Past month (n=553)	80.6% (446) (75.9% - 85.3%)	44.5% (246) (38.2% - 50.7%)	5.2% (29) (2.5% - 7.9%)	1.4% (8) (0.0% - 3.0%)
Overall (n=717)	78.2% (561) (73.9% - 82.5%)	43.7% (313) (38.2% - 49.2%)	6.3% (45) (3.7% - 8.8%)	1.4% (10) (0.1% - 2.6%)
‘Illegal’ States				
Past 12-months	60.6% (29) (34.1% - 87.1%)	46.1% (22) (17.6% - 74.6%)	9.1% (4) (0.0% - 22.9%)	1.8% (1) (0.0% - 5.6%)
Past month	67.2% (52) (51.4% - 82.9%)	74.0% (57) (60.2% - 87.9%)	7.6% (6) (0.0% - 16.7%)	1.2% (1) (0.0% - 3.6%)
Overall	64.7% (81) (51.2% - 78.2%)	63.3% (79) (50.0% - 76.6%)	8.2% (10) (0.8% - 15.6%)	1.4% (2) (0.0% - 3.4%)
‘Medical’ States				
Past 12-months	79.7% (25) (60.8% - 98.6%)	19.2% (6) (0.0% - 38.9%)	13.2% (4) (0.0% - 30.1%)	3.0% (1) (0.0% - 9.3%)
Past month	91.6% (166) (86.9% - 96.4%)	21.3% (39) (13.5% - 29.2%)	2.6% (5) (0.0% - 6.4%)	0.0% (0) (0.0% - 0.0%)
Overall	89.9% (191) (85.0% - 94.7%)	21.0% (45) (13.8% - 28.3%)	4.2% (9) (0.2% - 8.2%)	0.4% (1) (0.0% - 1.3%)

State ^a	Legal Methods of Euthanasia	Legal Restricted Uses	An Illegal Unqualified Use	Other Uses of Short Duration ^b
Fast 12 months	71.6% (69.3)	40.7% (41.1)	0.0% (0)	0.5% (0) ^c
	(39.0%, 37.6%)	(12.3%, 10.0%)	(1.0%, 10.0%)	(0.0%, 0.0%)
Fast 6 months	77.5% (220)	31.0% (208)	0.0% (0)	2.0% (7)
	(79.5%, 64.4%)	(42.0%, 36.0%)	(2.0%, 0.0%)	(0.0%, 0.0%)
Overall	73.9% (220)	35.0% (208)	0.0% (0)	0.7% (7)
	(70.0%, 82.0%)	(42.3%, 37.7%)	(1.0%, 0.0%)	(0.0%, 1.3%)

^a Response categories: "strongly agree", "agree", "disagree", "strongly disagree".

^b "Short duration" means less than 12 months.

^c "Other uses" means uses that are not legal, but are not illegal, such as uses that are not covered by the law.

^d "Fast 12 months" means "strongly agree" or "agree" to the statement "I would not use any of the methods listed above to end a patient's life." "Fast 6 months" means "strongly agree" or "agree" to the statement "I would not use any of the methods listed above to end a patient's life within 6 months." "Fast 12 months" and "Fast 6 months" are mutually exclusive.

^e Response options are not mutually exclusive; respondents may select as many as six of the six options.

2. Behavioral Risk Factor Surveillance System (BRFSS)

Table 63. Marijuana Use for Any Reason, Medical Reason, and Both Medical and Nonmedical Reason in the Past 30 Days in the Participating States/Territories, BRFSS, Marijuana Module, 2021

State/Territory*	Any Reason		Nonmedical Reason			Medical Reason			Both Medical and Nonmedical Reason		
	Frequency	Weighted Frequency (%)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)
Overall	17,666	8,017,412 (100)	5,700	2,905,432	36.2 (23.6, 26.2)	5,357	1,997,581	24.9 (23.6, 26.2)	6,609	3,114,399	38.8 (37.2, 40.5)
Alaska	863	93,885 (100)	368	44,102	47.0 (42.2, 51.7)	176	16,022	17.1 (14.0, 20.1)	319	33,761	36.0 (31.5, 40.4)
Connecticut	788	282,425 (100)	310	106,466	37.7 (33.1, 42.3)	175	57,045	20.2 (16.6, 23.8)	303	118,913	42.1 (37.1, 47.1)
Delaware	257	68,544 (100)	91	27,793	40.5 (32.6, 48.5)	88	21,125	30.8 (23.6, 38.0)	78	19,627	28.6 (21.7, 35.6)
Hawaii	748	106,338 (100)	215	32,495	30.6 (25.6, 35.5)	275	35,019	32.9 (28.1, 37.7)	258	38,824	36.5 (31.4, 41.6)
Idaho	401	106,816 (100)	128	36,134	33.8 (27.9, 39.8)	106	25,467	23.8 (18.7, 29.0)	167	45,215	42.3 (36.3, 48.4)
Illinois	290	1,026,164 (100)	126	425,699	41.5 (34.6, 48.3)	66	198,027	19.3 (14.1, 24.5)	98	402,438	39.2 (32.1, 46.4)
Indiana	566	369,827 (100)	187	128,361	34.7 (30.0, 39.4)	131	74,793	20.2 (16.5, 24.0)	248	166,674	45.1 (40.2, 50.0)
Kentucky	331	277,702 (100)	104	93,783	33.8 (27.8, 39.8)	90	64,935	23.4 (18.0, 28.8)	137	118,983	42.8 (36.2, 49.5)
Maine	2,577	413,256 (100)	669	110,925	26.8 (23.6, 30.1)	1,005	148,545	35.9 (32.5, 39.4)	903	153,786	37.2 (33.5, 40.9)
Maryland	2,034	883,969 (100)	510	240,704	27.2 (22.9, 31.5)	758	287,527	32.5 (28.0, 37.0)	766	355,739	40.2 (35.5, 45.0)
Minnesota	1,120	345,770 (100)	458	144,091	41.7 (38.2, 45.2)	272	80,123	23.2 (20.2, 26.2)	390	121,555	35.2 (31.8, 38.5)
Montana	645	112,874 (100)	179	31,185	27.6 (23.5, 31.7)	232	34,082	30.2 (25.9, 34.5)	234	47,607	42.2 (37.3, 47.0)
Nebraska	286	94,743 (100)	114	40,236	42.5 (35.0, 50.0)	61	17,716	18.7 (13.6, 23.8)	111	36,791	38.8 (31.5, 46.2)

State/Territory*	Any Reason		Nonmedical Reason			Medical Reason			Both Medical and Nonmedical Reason		
	Frequency	Weighted Frequency (%)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)
Nevada	358	359,031 (100)	138	144,810	40.3 (33.3, 47.4)	87	87,766	24.4 (17.7, 31.2)	133	126,455	35.2 (28.4, 42.0)
New Hampshire	486	120,462 (100)	183	47,227	39.2 (33.5, 44.9)	126	23,774	19.7 (15.6, 23.9)	177	49,460	41.1 (35.3, 46.8)
New York	1,208	1,611,364 (100)	477	788,848	49.0 (44.3, 53.6)	255	210,651	13.1 (10.5, 15.7)	476	611,864	38.0 (33.4, 42.6)
North Dakota	303	44,161 (100)	105	16,206	36.7 (29.9, 43.5)	97	12,870	29.1 (22.9, 35.4)	101	15,085	34.2 (27.4, 40.9)
Ohio	1,592	866,871 (100)	431	251,600	29.0 (24.9, 33.2)	512	243,665	28.1 (24.0, 32.2)	649	371,606	42.9 (38.3, 47.4)
Oklahoma	273	401,216 (100)	26	50,448	12.6 (6.9, 18.2)	175	244,845	61.0 (53.6, 68.4)	72	105,924	26.4 (19.9, 32.9)
Rhode Island	620	118,445 (100)	194	36,350	30.7 (25.7, 35.7)	159	26,989	22.8 (18.3, 27.3)	267	55,106	46.5 (41.1, 51.9)
Utah	659	184,017 (100)	168	51,998	28.7 (24.2, 33.1)	244	61,415	33.8 (29.4, 38.3)	241	68,068	37.5 (32.9, 42.1)
Vermont	1,006	97,963 (100)	422	43,946	44.9 (40.3, 49.4)	197	15,572	15.9 (12.9, 18.9)	387	38,445	39.2 (34.8, 43.7)
Wyoming	146	22,624 (100)	49	8,427	37.2 (26.4, 48.1)	41	5,192	23.0 (14.1, 31.8)	53	9,005	39.8 (29.1, 50.6)
Guam	118	11,481 (100)	48	3,597	31.3 (18.3, 44.4)	29	4,416	38.5 (22.1, 54.8)	41	3,467	30.2 (17.9, 42.5)

* Excludes individuals who responded, "Don't know/not sure" and those who refused to answer.

Table 64. Past 30-Day Marijuana Use by Method of Use and Stratified by Reason of Use, BRFSS, Marijuana Module, 2021

Method of Use*	Any Reason		Recreational Reason			Medical Reason			Both Medical and Nonmedical		
	Frequency	Weighted Frequency (%)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)	Frequency	Weighted Frequency	Weighted % (95% CI)
Any	17,605	7,971,458	5,679	2,884,067	100	5,334	1,989,539	100	6,592	3,097,852	100
Smoke	11,684	5,453,712	3,881	1,963,413	68.1 (65.4, 70.8)	2,961	1,200,016	60.3 (57.5, 63.1)	4,842	2,290,283	73.9 (71.6, 76.3)
Eat	3,408	1,370,291	1,171	555,280	19.3 (16.9, 21.6)	1,354	424,142	21.3 (19.1, 23.5)	883	390,868	12.6 (10.7, 14.5)
Drink	170	58,107	39	13,981	0.5 (0.2, 0.8)	84	30,421	1.5 (0.8, 2.3)	47	13,705	0.4 (0.2, 0.7)
Vaporize	1,561	760,394	469	287,442	10.0 (8.3, 11.7)	542	202,612	10.2 (8.5, 11.8)	550	270,340	8.7 (7.2, 10.2)
Dab	404	183,290	74	34,688	1.2 (0.8, 1.6)	113	44,979	2.3 (1.5, 3.1)	217	103,623	3.3 (2.5, 4.2)
Other	378	145,664	45	29,263	1.0 (0.3, 1.7)	280	87,368	4.4 (3.2, 5.6)	53	29,033	0.9 (0.5, 1.4)

* Excludes individuals who responded, "Don't know/not sure" and those who refused to answer.

3. Monitoring the Future (MTF)

Table 65. Sample Size and Response Rate, MTF, 2017–2022

Year	Number of Students				Response Rate (%)		
	8th Grade	10th Grade	12th Grade	Total	8th Grade	10th Grade	12th Grade
2017	16,010	14,171	13,522	43,703	87	85	79
2018	14,836	15,144	14,502	44,482	89	86	81
2019	14,223	14,595	13,713	42,531	89	86	80
2020	3,161	4,890	3,770	11,821	88	89	79
2021	11,446	11,792	9,022	32,260	82	78	69
2022	9,889	11,950	9,599	31,438	86	84	75

4. State Data From State Medical Marijuana Programs

4.1. Maryland Medical Cannabis Patient Survey 2022 (MMCPS-22)

Cannabis Public Policy Consulting, Quality Control Processes (Excerpt From the CPPC Project Proposal)

Quality control is built into our projects in a variety of ways, beginning with the assignment of record keeping to one researcher (“record keeper”), who is the single owner of documentation for the project. Key personnel on the project will [be] able to access files necessary to complete work through permission settings, but all changes to files and documents must be approved [by] the record keeper to ensure quality control. This prohibits the duplication of files, the corruption of files, or compromising of critical data when multiple personnel are working in one document from separate computers. The record keeper follows Cannabis Public Policy Consulting (CPPC)’s standard operating procedures for documentation, such as keeping consistent naming conventions for files and encrypting documentation with passwords when necessary.

Additionally, the record keeper is responsible for routine quality control checks throughout the survey administration period. These checks will ensure representativeness of the sample, identify system errors or failures, confirm patient privacy, and protect data integrity.

These checks will include, but not be limited to, the following actions:

- (1) Review geographic and demographic participation data during the survey collection period to ensure sampling is representative in an ongoing fashion (i.e., ensure there are no hotspots that compromise representation early on).
- (2) Ensure that the questionnaire is at a reading level approved by the client and 508 compliant if deemed necessary.
- (3) Perform multiple quality assurance checks on data analysis and all data cleaning performed and verified by key personnel individually.
- (4) Guarantee that the questionnaire language is equitable when capturing demographic data (i.e., providing adequate options for pronouns, gender identities, and race/ethnicity).

- (5) Perform test runs on survey links, databases, and other systems used for data collection, storage, and analysis.
- (6) For all analysis, run statistical methods three individual times to make sure outcome and finding is consistent prior to final documentation.
- (7) Back up all files and data documentation every 24 hours.
- (8) Perform other checks requested in collaboration by the State of Maryland and CPPC.

Should an error be discovered through any of the quality control checks or quality control procedures built into the project, the record keeper will document the error and provide this notification in writing to the Contract Monitor. CPPC commits itself to remedying all issues within 5 days of notification at no cost to the Commission. All correction actions will be thoroughly documented and provided to the Commission upon remediation. Further, CPPC commits itself to seeking the appropriate approval process prior to taking corrective actions as to ensure the Commission has agreed to and approved the next steps and remediation procedures as outlined in the Problem Escalation Procedure in Section 3.8 [of the CPPC project proposal].

4.2. Maryland Medical Cannabis Commission (MMCC) Tables

Table 66. Descriptive Characteristics of Maryland Medical Cannabis Commission (MMCC) Survey Participants

Characteristic	N	%
Age in Years		
18-20	206	1.6
21-25	676	5.2
26-35	2674	20.6
36-45	3140	24.1
46-55	2245	17.3
56-65	2207	17
66-75	1665	12.8
76-85	181	1.4
86+	16	0.1
Gender Identity		
Male	5684	43.7
Female	6994	53.8
Transgender female	25	0.2
Transgender male	35	0.3
Non-binary	161	1.2
Not included in above	12	0.1
Prefer not to answer	100	0.8
Race		
White or Caucasian	10181	78.2
Black or African American	1778	13.7
Asian	153	1.2
Native Hawaiian or Other Pacific Islander	19	0.1
American Indian or Alaskan Native	69	0.5
Not included above	376	2.9
More than one race	330	2.5

Characteristic	N	%
Ethnicity		
Hispanic or Latino	813	6.2
Not Hispanic or Latino	12185	93.7
Missing	13	
Highest Level of Education		
Less than high school	165	1.3
High school or equivalent	2159	16.6
Trade school certificate/diploma	743	5.7
Some college, or associates degree	4177	32.1
Bachelor's degree	3241	24.9
Master's degree, doctoral degree (e.g, PhD, MD, etc.)	2524	19.4
Missing	2	
Medicaid Enrollment Status		
Not currently enrolled	10311	79.2
Currently enrolled	2187	16.8
Employment Status		
Working full-time	7285	56
Working part-time	1078	8.3
Student	234	1.8
Stay-at-home parent or homemaker	594	4.6
Not working	689	5.3
Not working, seeking employment	370	2.8
Retired	2350	18.1
Missing	411	
Annual Household Income		
No income	222	1.7
Less than \$14,000	567	4.4
\$14,000 to \$29,999	1086	8.3
\$30,000 - \$49,999	1786	13.7
\$50,000 - \$74,999	2000	15.4
\$75,000 - \$99,000	1612	12.4
\$100,000 to \$150,000	2176	16.7
\$150,000 - \$200,000	1099	8.4
More than \$200,000	987	7.6
Prefer not to answer	1227	9.4
Sensory or Physical Disability		
Serious difficulty hearing	761	5.8
Serious difficulty seeing, even when wearing glasses	645	5
Serious difficulty concentrating or making decisions due to a physical, mental, or emotional condition	2312	17.8
Serious difficulty walking or climbing stairs	1730	13.3
Serious difficulty bathing or dressing	384	3
Serious difficulty doing errands alone	1257	9.7
Years of Certification in the Maryland Medical Cannabis Program		
1	3721	28.6
2	3397	26.1
3	3233	24.8
4	1630	12.5
5	893	6.9

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 67. Frequencies of Substance Use in the Past Month Maryland Medical Cannabis Commission (MMCC) Survey Participants

Frequency of Substance Use	N	%
Cannabis		
0 days	521	4
1-4 days	1134	8.7
5-10 days	1216	9.3
11-19 days	1652	12.7
20-29 days	2602	20
All 30 days	5868	45.1
Tobacco		
0 days	10095	77.6
1-4 days	430	3.3
5-10 days	231	1.8
11-19 days	233	1.8
20-29 days	252	1.9
All 30 days	1693	13
Alcohol		
0 days	5207	40
1-4 days	3784	29.1
5-10 days	1975	15.2
11-19 days	1168	9
20-29 days	569	4.4
All 30 days	259	2
Psychedelics		
0 days	12453	95.7
1-4 days	409	3.1
5-10 days	30	0.2
11-19 days	10	0.1
20-29 days	3	0
All 30 days	27	0.2
Benzodiazepines		
0 days	11774	90.5
1-4 days	526	4
5-10 days	176	1.4
11-19 days	77	0.6
20-29 days	66	0.5
All 30 days	313	2.4
Stimulants		
0 days	12178	93.6
1-4 days	168	1.3
5-10 days	85	0.7
11-19 days	74	0.6
20-29 days	130	1
All 30 days	295	2.3
Opioids		
0 days	12306	94.6
1-4 days	175	1.3
5-10 days	67	0.5
11-19 days	48	0.4
20-29 days	42	0.3
All 30 days	284	2.2

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 68. Methods of Cannabis Administration (One Time or More) in the Past Month Maryland Medical Cannabis Commission (MMCC) Survey Participants

Method of Cannabis Administration	n	%
Flower or smoked dried herb	9375	72.1
Cartridge/Vaporizer	7978	61.3
Concentrate	2294	17.6
Edibles	8630	66.3
Capsules or tablets	1575	12.1
Tinctures or oral sprays	1597	12.3
Topicals	2879	22.1
Transdermal patch	177	1.4
Rectal/Vaginal suppositories	64	0.5

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 69. Perceived Effectiveness of Cannabis Treatment, Maryland Medical Cannabis Commission (MMCC) Survey Participants

Perceived Effectiveness	n	%
Not effective at all	70	0.5
Slightly effective	447	3.4
Moderately effective	2782	21.4
Very effective	5981	46
Extremely effective	3648	28.2

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 70. Perceived Health and Social Effects of Cannabis Among Maryland Medical Cannabis Commission (MMCC) Survey Participants

Perceived Effect	Worsened		Improved		Neither	
	n	%	n	%	n	%
Physical health	127	1	9359	71.9	3444	26.5
Mood or mental health	64	0.5	11527	88.6	1338	10.3
Memory or concentration	998	7.7	4817	37	7109	54.6
Social relationships	107	0.8	7064	54.3	5758	44.3

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 71. Frequency of Conditions While Consuming Cannabis Among Maryland Medical Cannabis Users

Condition	Never		Once		About Monthly		About Weekly		About Daily	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Anxiety	8965	68.9	1995	15.3	1122	8.6	473	3.6	352	2.7
Panic	10784	82.9	1270	9.8	527	4.1	184	1.4	143	1.1
Psychotic or paranoid feelings	11238	86.4	1044	8	433	3.3	119	0.9	74	0.6
Suicidal thoughts or ideation	12538	96.4	168	1.3	116	0.9	45	0.3	40	0.3
Breathing problems	11593	89.1	691	3.9	397	3.1	146	1.1	73	0.6
Nausea/vomiting	11726	90.1	740	5.7	255	2	102	0.8	71	0.5

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 72. Symptoms Experienced by Maryland Medical Cannabis Users in the Past Six Months, Maryland Medical Cannabis Commission (MMCC) Survey Participants

Survey Question on Symptoms	Never		Sometimes		About Half the Time		Most of the Time		Always	
	n	%	n	%	n	%	n	%	n	%
Had a problem with memory or concentration after using cannabis?	8473	65.1	3818	29.3	348	2.7	205	1.6	65	0.5
Devoted a great deal of time to getting, using, or recovering from cannabis?	11362	87.3	1241	9.5	172	1.3	86	0.7	39	0.3
Felt like you are not in control of your cannabis consumption or could not reduce your consumption even when you wanted to?	11880	91.3	712	5.5	110	0.8	85	0.7	91	0.7

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 73. Frequency of Treatment in an Emergency Room or Urgent Care Facility for Any Reason Related to Cannabis Consumption Among Maryland Medical Cannabis Users

Frequency	n	%
Never	12784	98.3
Once	96	0.7
Twice	27	0.2
Three times	10	0.1
More than three times	9	0.1
Total	12926	

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

Table 74. Frequency of Driving Within Three Hours of Consuming Cannabis and/or Under the Influence of Cannabis in the Past Month Among Maryland Medical Cannabis Patients

Frequency	n	%
0 times	10382	79.8
1 time	482	3.7
2-3 times	835	6.4
4-5 times	226	1.7
6 or more times	831	6.4
Total	12756	

Source: Maryland Medical Cannabis Commission in a report dated March 7, 2023.

4.3. Minnesota Tables

Table 75. Qualifying Medical Conditions for Medical Cannabis Use in Minnesota

Condition
Alzheimer's disease
Amyotrophic lateral sclerosis (ALS)
Autism spectrum disorder (must meet Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-5])
Cancer (If illness or its treatment produces one or more of the following: severe or chronic pain; nausea or severe vomiting; or cachexia or severe wasting.)
Chronic motor or vocal tic disorder
Chronic pain
Glaucoma
HIV/AIDS
Inflammatory bowel disease, including Crohn's disease
Intractable pain
Irritable bowel syndrome (effective Aug. 1, 2023)
Obsessive-compulsive disorder (effective Aug. 1, 2023)
Obstructive sleep apnea
Post-traumatic stress disorder (PTSD)
Seizures, including those characteristic of epilepsy
Severe and persistent muscle spasms, including those characteristic of multiple sclerosis (MS)
Sickle cell disease
Terminal illness, with a probable life expectancy of less than one year (If illness or its treatment produces one or more of the following: severe or chronic pain; nausea or severe vomiting; or cachexia or severe wasting.)
Tourette syndrome

Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

Table 76. Minnesota Survey Responses and Most Common Adverse Events (AEs) for 2015-2017

Year	Response Rate	# Patients	# Experiencing AEs	Degree of AEs	Most Common AEs
2015-2016	91%	1,502	272 (18%)	The majority (91%) of side effect responses were reported to be mild or moderate in severity	Dry mouth (3.9%), drowsiness/somnolence/sedation (3.9%), and fatigue (3.5%).
2016-2017	96%	5,412	759 (14%)	90% (N = 1,421) of the 1,584 side effect responses were mild (n = 758; 48%) or moderate (n = 663; 42%) in severity	Dry mouth (4.1%), fatigue (3%), drowsiness/somnolence/sedation (3%), and mental clouding/"foggy brain" (3%)

Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

Table 77. Frequencies of Side Effects Reported Among Minnesota Medical Cannabis Patients by Year and Severity, 2017-2022

Year	Number of Patient Completed Surveys	Number Reporting Any Side Effect (% of Patient Surveys)	Number Reporting Severe Side Effect (% of Patient Surveys)	Number Reporting Moderate Side Effect (% of Patient Surveys)	Number Reporting Mild Side Effect (% of Patient Surveys)
2017	34140	2805 (8.22)	252 (0.74)	988 (2.89)	1565 (4.58)
2018	86196	6627 (7.69)	681 (0.79)	2305 (2.67)	3641 (4.22)
2019	125995	9001 (7.14)	808 (0.64)	2967 (2.35)	5226 (4.15)
2020	152861	7654 (5.01)	575 (0.38)	2231 (1.46)	4848 (3.17)
2021	192719	10681 (5.54)	595 (0.31)	3204 (1.66)	6882 (3.57)
2022	357078	15656 (4.38)	793 (0.22)	4254 (1.19)	10609 (2.97)

Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

Table 78. Top Ten Side Effects Reported on the MN Patient Self-Evaluation by Year (2017-2022)

Side Effect	Number of Patient Reports	% of Patient Reports
2017		
Dry mouth	636	1.86
Mental clouding/"foggy brain"	287	0.84
Other	273	0.80
Drowsiness/somnolence/sedation	218	0.64
Fatigue	218	0.64
Increased appetite	206	0.60
Euphoria (intense feeling of well-being or pleasure)	85	0.25
Dizziness	82	0.24
Nausea	75	0.22
Difficulty concentrating	71	0.21
2018		
Dry mouth	1421	1.65
Mental clouding/"foggy brain"	600	0.7
Drowsiness/somnolence/sedation	570	0.66
Other	548	0.64
Fatigue	526	0.61
Increased appetite	467	0.54
Dizziness	312	0.36
Headache	252	0.29
Lightheadedness	212	0.25
Anxiety	175	0.2

Side Effect	Number of Patient Reports	% of Patient Reports
2019		
Dry mouth	2151	1.71
Mental clouding/"foggy brain"	898	0.71
Drowsiness/somnolence/sedation	777	0.62
Other	727	0.58
Fatigue	698	0.55
Increased appetite	669	0.53
Dizziness	384	0.3
Lightheadedness	314	0.25
Headache	272	0.22
Anxiety	225	0.18
2020		
Dry mouth	2134	1.4
Increased appetite	687	0.45
Mental clouding/"foggy brain"	687	0.45
Fatigue	640	0.42
Drowsiness/somnolence/sedation	616	0.4
Other	551	0.36
Dizziness	302	0.2
Lightheadedness	196	0.13
Headache	188	0.12
Euphoria (intense feeling of well-being or pleasure)	176	0.12
2021		
Dry mouth	3213	1.67
Increased appetite	999	0.52
Mental clouding/"foggy brain"	911	0.47
Drowsiness/somnolence/sedation	863	0.45
Other	827	0.43
Fatigue	746	0.39
Dizziness	448	0.23
Headache	303	0.16
Euphoria (intense feeling of well-being or pleasure)	279	0.14
Lightheadedness	250	0.13
2022		
Dry mouth	5823	1.63
Other	1347	0.38
Increased appetite	1295	0.36
Mental clouding/"foggy brain"	1234	0.35
Drowsiness/somnolence/sedation	969	0.27
Fatigue	943	0.26
Dizziness	488	0.14
Headache	429	0.12
Anxiety	376	0.11
Lightheadedness	315	0.09

Source: Estimates generated by FDA using data provided by Minnesota Department of Health April 3, 2023 and April 12, 2023.

Table 79. Patient Numbers by State: 2016-2020 (Only States With Available Data)

State	2016	2017	2018	2019	2020
Alaska	1084	1053	621	404	NR
Arizona	114439	152979	186002	219817	295295
Arkansas	NR	NR	5459	15351	66638
Colorado	94577	93372	86641	81610	85814
Connecticut	15136	22573	26641	36700	49562
Delaware	1414	3274	6060	11213	15495
Florida	NR	42724	167211	299914	456594
Hawaii	15334	19858	23746	27152	30868
Illinois	7707	21800	39808	76939	121775
Louisiana	NR	NR	NR	4350	NR
Maryland	NR	11489	51589	90120	121994
Massachusetts	33543	45319	58920	60110	92240
Michigan	218556	269553	297515	268566	243372
Minnesota	2806	8075	14481	18249	28522
Missouri	NR	NR	NR	22706	69397
Montana	7785	22849	31186	36422	41638
Nevada	25358	23489	17211	15839	13303
New Hampshire	2089	3493	6480	8302	10688
New Jersey	12154	16937	44000	63062	81111
New Mexico	29046	46645	67574	80257	104655
New York	4998	57960	98101	111358	133362
North Dakota	NR	NR	0	707	3233
Ohio	NR	NR	3575	78376	176387
Oklahoma	NR	NR	30786	238869	367053
Oregon	68032	50400	31251	24801	22603
Pennsylvania	NR	10532	100027	243433	297317
Rhode Island	16418	18533	16963	16218	19803
Utah	NR	NR	NR	NR	16096
Vermont	3332	5313	NR	NR	NR
Washington DC	4600	5386	5836	6160	9618
Total	661990	953606	1417684	2157005	2974433

Source: University of Michigan tabulation of state annual reports, provided to the FDA on February 28, 2023.

Abbreviations: NR, not reported

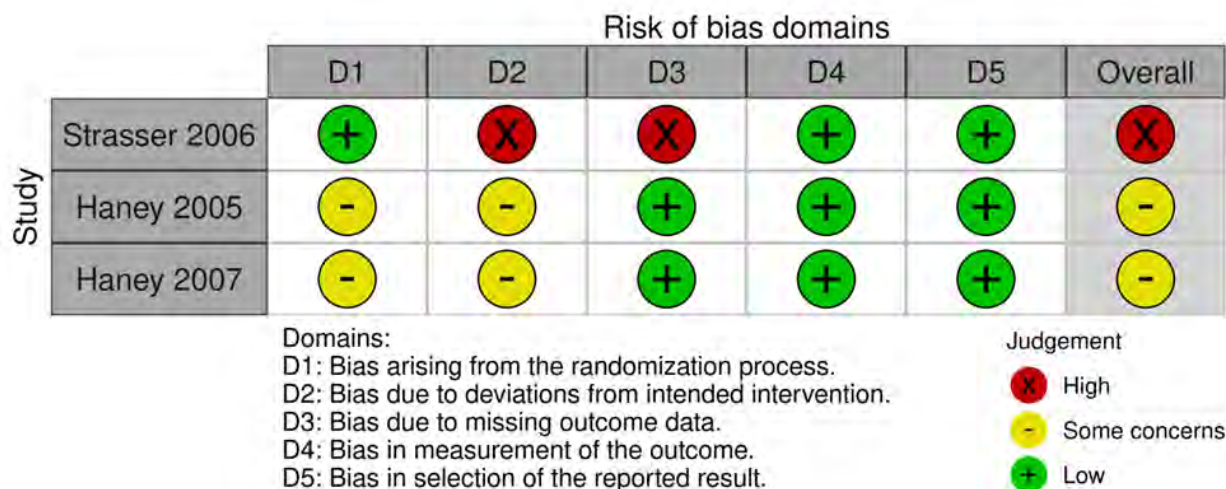
5. Tables and Figures Exempted from University of Toronto's
Systematic Review of the Medical Literature on Cannabis Use

5.1. Summary

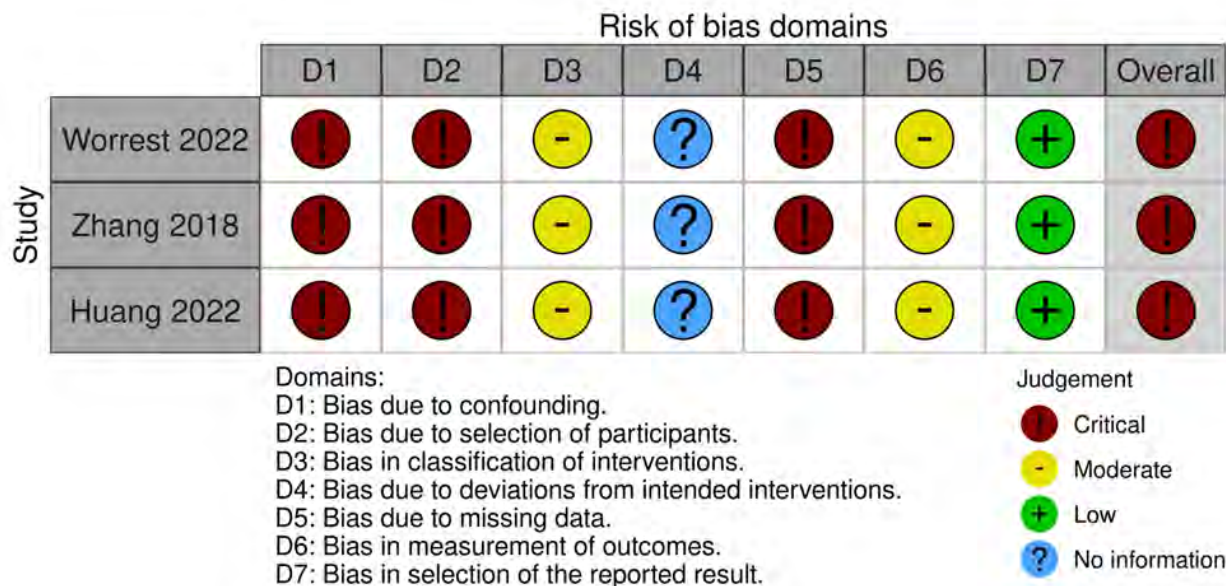
Table/Figure	Exempted	Reason
Table 1: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 1: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Table 2: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 2: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Table 3: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 3: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act

5.2. Detailed Description of Exempted Tables and Figures

Table/Figure	Exempted	Reason
Table 1: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 1: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Table 2: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 2: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Table 3: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act
Figure 3: Summary of Exempted Tables and Figures	Yes	Exempted under the Access to Information Act

Figure 14. Risk of Bias Assessment, Randomized Clinical Trials, Anorexia

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Figure 15. Risk of Bias Assessment, Observational Studies, Anorexia

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

5.2. Anxiety

Table 82. Summary of Included Studies for Anxiety

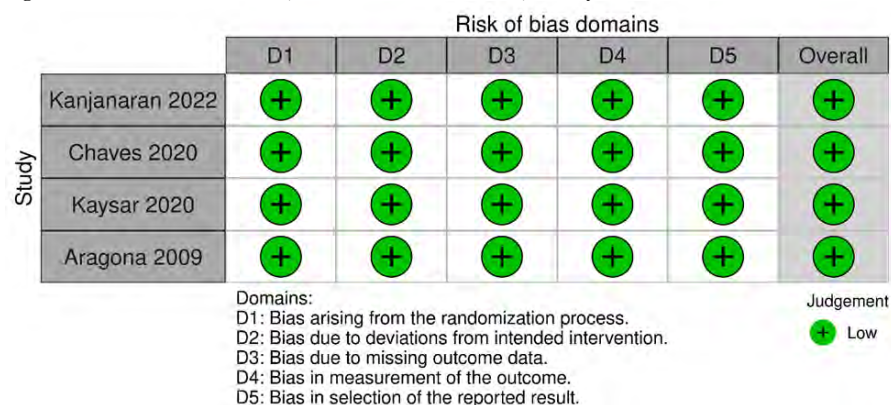
Study Type	Count of Included Studies	Notes
Randomized controlled trials (RCTs)	3	---
Observational studies	0	---
Systematic reviews (SRs)	25	---
Eligible RCTs identified from SRs	1	Duplicate included studies not reported
Eligible observational studies identified from SRs	1	Duplicate included studies not reported
Total non-eligible studies identified from SRs	299	Unique component studies
Total studies included in risk of bias assessments	5	SRs not included in quantitative synthesis

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

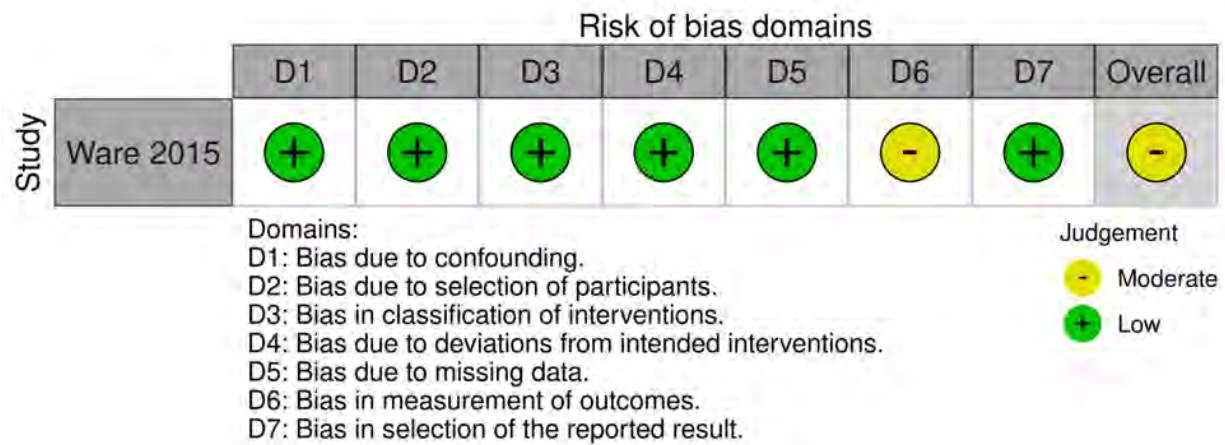
Table 83. References (Studies Included in Risk of Bias Assessments, Anxiety)

Randomized Clinical Trials	
1	(Chaves et al. 2020)
2	(Kayser et al. 2020)
3	(Aragona et al. 2009)
4	(Kanjanaarangsichai et al. 2022)
Observational Studies	
1	(Ware et al. 2015)

Figure 16. Risk of Bias Assessment, Randomized Clinical Trials, Anxiety



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Figure 17. Risk of Bias Assessment, Observational Studies, Anxiety

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

5.3. Inflammatory Bowel Disease

Table 10. Summary of Selected Studies for Inflammatory Bowel Disease

Study Title	Level of Evidence	Included Studies	Notes
Observational studies	4	1	IBD was associated with administration of oral contraceptive estrogens, and risk of relapse was increased in women using oral contraceptives. However, the association of IBD with oral contraceptive use was not statistically significant. IBD was more likely to be diagnosed in women who had used oral contraceptives in the previous 12 months.
Randomized studies	1a	2	1. Oral contraceptive use was associated with increased risk of relapse in Crohn's disease. 2. Oral contraceptive use was associated with increased risk of relapse in Crohn's disease.
Controlled studies	2	1	Oral contraceptive use was associated with increased risk of relapse in Crohn's disease.

Note: IBD = inflammatory bowel disease; Crohn's = Crohn's disease; UC = ulcerative colitis.

Source: Adapted from *Medical Progress in Crohn's Disease and Ulcerative Colitis*, 2004, by J. S. Hyman, M. S. Fennerty, and J. S. Hyman. Copyright © 2004 by Humana Press, Inc. All rights reserved.

Table 11. Side Effects of Oral Contraceptives in Women with Inflammatory Bowel Disease

Side Effect	Study
1. Increased risk of relapse in Crohn's disease	1
2. Increased risk of relapse in Crohn's disease	2
3. Increased risk of relapse in Crohn's disease	3
4. Increased risk of relapse in Crohn's disease	4
5. Increased risk of relapse in Crohn's disease	5
6. Increased risk of relapse in Crohn's disease	6
7. Increased risk of relapse in Crohn's disease	7
8. Increased risk of relapse in Crohn's disease	8
9. Increased risk of relapse in Crohn's disease	9
10. Increased risk of relapse in Crohn's disease	10
11. Increased risk of relapse in Crohn's disease	11
12. Increased risk of relapse in Crohn's disease	12
13. Increased risk of relapse in Crohn's disease	13
14. Increased risk of relapse in Crohn's disease	14
15. Increased risk of relapse in Crohn's disease	15
16. Increased risk of relapse in Crohn's disease	16
17. Increased risk of relapse in Crohn's disease	17
18. Increased risk of relapse in Crohn's disease	18
19. Increased risk of relapse in Crohn's disease	19
20. Increased risk of relapse in Crohn's disease	20
21. Increased risk of relapse in Crohn's disease	21
22. Increased risk of relapse in Crohn's disease	22
23. Increased risk of relapse in Crohn's disease	23
24. Increased risk of relapse in Crohn's disease	24
25. Increased risk of relapse in Crohn's disease	25
26. Increased risk of relapse in Crohn's disease	26
27. Increased risk of relapse in Crohn's disease	27
28. Increased risk of relapse in Crohn's disease	28
29. Increased risk of relapse in Crohn's disease	29
30. Increased risk of relapse in Crohn's disease	30
31. Increased risk of relapse in Crohn's disease	31
32. Increased risk of relapse in Crohn's disease	32
33. Increased risk of relapse in Crohn's disease	33
34. Increased risk of relapse in Crohn's disease	34
35. Increased risk of relapse in Crohn's disease	35
36. Increased risk of relapse in Crohn's disease	36
37. Increased risk of relapse in Crohn's disease	37
38. Increased risk of relapse in Crohn's disease	38
39. Increased risk of relapse in Crohn's disease	39
40. Increased risk of relapse in Crohn's disease	40
41. Increased risk of relapse in Crohn's disease	41
42. Increased risk of relapse in Crohn's disease	42
43. Increased risk of relapse in Crohn's disease	43
44. Increased risk of relapse in Crohn's disease	44
45. Increased risk of relapse in Crohn's disease	45
46. Increased risk of relapse in Crohn's disease	46
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50. Increased risk of relapse in Crohn's disease	50
51. Increased risk of relapse in Crohn's disease	51
52. Increased risk of relapse in Crohn's disease	52
53. Increased risk of relapse in Crohn's disease	53
54. Increased risk of relapse in Crohn's disease	54
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89. Increased risk of relapse in Crohn's disease	89
90. Increased risk of relapse in Crohn's disease	90
91. Increased risk of relapse in Crohn's disease	91
92. Increased risk of relapse in Crohn's disease	92
93. Increased risk of relapse in Crohn's disease	93
94. Increased risk of relapse in Crohn's disease	94
95. Increased risk of relapse in Crohn's disease	95
96. Increased risk of relapse in Crohn's disease	96
97. Increased risk of relapse in Crohn's disease	97
98. Increased risk of relapse in Crohn's disease	98
99. Increased risk of relapse in Crohn's disease	99
100. Increased risk of relapse in Crohn's disease	100

Figure 18. Risk of Bias Assessment, Randomized Clinical Trials, Inflammatory Bowel Disease

		Risk of bias domains					Overall
		D1	D2	D3	D4	D5	
Study	Naftali 2013	-	X	+	+	-	X
	Naftali 2021a	+	-	+	+	X	X
	Irving 2018	+	+	X	+	X	X
	Naftali 2021b	+	-	+	X	X	X

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
X High
- Some concerns
+ Low

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Figure 19. Risk of Bias Assessment, Observational Studies, Inflammatory Bowel Disease

		Risk of bias domains							Overall
		D1	D2	D3	D4	D5	D6	D7	
Study	Desai 2020	!	X	!	?	+	-	?	!
	Desai 2019	!	X	!	?	+	-	?	!
	Mbachii 2019a	!	!	!	?	X	X	?	!
	Mbachii 2019b	!	!	!	?	X	X	?	!
	Coates 2022	X	X	X	?	+	-	?	X
	Choi 2022	-	X	X	?	X	-	+	X

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
! Critical
X Serious
- Moderate
+ Low
? No information

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

5.4. Nausea

Table 86. Summary of Included Studies for Nausea

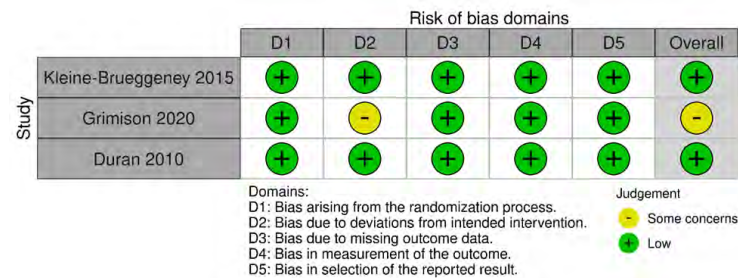
Study Type	Count of Included Studies	Notes
Randomized controlled trials (RCTs) obtained from literature search	3	---
Observational studies obtained from literature search	0	---
Total studies included in risk of bias assessments	3	---

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 87. References (Studies Included in Risk of Bias Assessments, Nausea)

Randomized Clinical Trials	
1	(Grimison et al. 2020)
2	(Kleine-Brueggeneay et al. 2015)
3	(Duran et al. 2010)

Figure 20. Risk of Bias Assessment, Randomized Clinical Trials, Nausea



Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

5.5. Pain

Table 88. Summary of Included Studies for Pain

Study Type	Count of Included Studies	Notes
Randomized controlled trials (RCTs)	32	Total RCTs remaining following review of exposure criteria
Observational studies	6	Total Observational studies remaining following review of exposure criteria
Systematic reviews (SRs)	66	---
Eligible RCTs identified from SRs	7	Duplicate included studies not reported
Eligible observational studies identified from SRs	2	Duplicate included studies not reported
Total non-eligible studies identified from SRs	313	Unique component studies
Total studies included in risk of bias assessments	47	SRs not included in quantitative synthesis

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Table 89. References (Studies Included in Risk of Bias Assessments, Pain)

Randomized Clinical Trials	
1	(Corey-Bloom et al. 2012)
2	(Weizman et al. 2018)
3	(Abrams et al. 2007)
4	(Wilsey et al. 2008)
5	(Wallace et al. 2015)
6	(Wilsey et al. 2013)
7	(van de Donk et al. 2019)
8	(Wallace et al. 2020)
9	(Conte et al. 2009)
10	(Notcutt et al. 2004)
11	(Buggv et al. 2003)
12	(Selvarajah et al. 2010)
13	(Zajicek et al. 2012)
14	(van Amerongen et al. 2018)
15	(Zubcevic et al. 2023)
16	(Gilman et al. 2022)
17	(Lichtman et al. 2018)
18	(Portenoy et al. 2012)
19	(Langford et al. 2013)
20	(Johnson et al. 2010)
21	(Marinelli et al. 2022)
22	(Meuth et al. 2020)
23	(Lynch et al. 2014)
24	(Nurmikko et al. 2007)
25	(Wilsey et al. 2016b)
26	(Wilsey et al. 2016a)
27	(Zylla et al. 2021)
28	(Blake et al. 2006)
29	(Chaves et al. 2020)
30	(de Vries et al. 2016)
31	(de Vries et al. 2017)
32	(Ellis et al. 2009)
33	(Ware et al. 2010)
34	(Zajicek et al. 2003)



Figure 21. Risk of Bias Assessment, Randomized Clinical Trials, Pain

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Abrams 2007	+	+	+	+	+	+
Buggy 2003	+	+	+	+	-	+
Chaves 2020	-	+	+	+	+	-
Corey-Bloom 2012	+	+	+	+	+	+
De Vries 2016a	+	+	+	+	+	+
De Vries 2016b	+	+	-	+	+	+
Ellis 2009	+	-	+	+	+	-
Gilman 2022	-	X	+	-	+	X
Jefferson 2013	X	-	+	+	X	X
Johnson 2010	+	+	+	+	+	+
Marinelli 2022	+	-	-	+	+	-
Meuth 2022	-	+	+	+	+	+
van Amerongen 2018	+	+	+	+	+	+
van de Donk 2019	-	-	X	X	X	X
Wallace 2020	+	+	+	+	+	+
Wallace 2015	-	+	+	X	+	X
Ware 2010	-	+	+	+	+	-
Wilsey 2013	+	-	+	+	+	-
Wilsey 2008	X	-	+	+	+	X
Zajicek 2012	+	+	+	+	+	+
Zubcevik 2022	+	+	+	+	-	+
Zylla 2021	-	+	-	+	+	-
Wilsey 2016a	+	+	+	+	+	+
Conte 2009	+	+	+	+	+	+
Blake 2005	-	X	-	+	+	X
Langford 2012	+	+	+	-	+	-
Lichtman 2018	-	-	+	+	+	-
Nurmikko 2007	+	+	-	+	-	-
Selvarajah 2009	-	-	+	+	+	-
Lynch 2014	+	X	X	X	-	X
Portenoy 2012	+	+	-	+	+	+
Wilsey 2016b	+	+	+	+	+	+
Zajicek 2003	+	-	+	+	-	-
Weizman 2018	+	-	+	+	+	-
Abrams 2020	+	+	+	+	+	+
Berman 2004	+	+	-	-	+	-
Almog 2020	+	+	+	+	-	-
Notcutt 2004	+	X	+	+	+	X
Naftali 2013	-	X	+	+	-	X

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
High
Some concerns
Low

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Figure 22. Risk of Bias Assessment, Observational Studies, Pain

		Risk of bias domains							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Pawasarat 2020	!	X	+	?	+	-	+	!
	Wilson 2020	X	!	+	?	!	+	X	!
	Sharma 2022	!	+	+	-	-	-	-	!
	Habib 2018	!	X	X	?	-	-	+	!
	Fiz 2011	X	!	X	-	?	+	X	X
	Horthoj 2022	X	-	+	?	!	+	+	!
	Zhang 2018	!	!	-	?	!	-	+	!
	Ware 2015	+	+	+	+	+	-	+	-

Domains:

D1: Bias due to confounding.

D2: Bias due to selection of participants.

D3: Bias in classification of interventions.

D4: Bias due to deviations from intended interventions.

D5: Bias due to missing data.

D6: Bias in measurement of outcomes.

D7: Bias in selection of the reported result.

Judgement

! Critical

X Serious

- Moderate

+

Low

?

No information

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

5.6. Post-Traumatic Stress Disorder

What are the symptoms of Post-Traumatic Stress Disorder?

Category	Number of symptoms
Re-experiencing trauma (PTSD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (PTSD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: PTSD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Acute Stress Disorder?

Category	Number of symptoms
Re-experiencing trauma (ASD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (ASD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: ASD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Complex Post-Traumatic Stress Disorder?

Category	Number of symptoms
Re-experiencing trauma (CPTSD)	1
Avoidance	2
Hyperarousal	3
Negative changes in thinking and feeling	4
Changes in relationships	5

Re-experiencing trauma (CPTSD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Negative changes in thinking and feeling

- 1. Negative changes in thinking and feeling about the world
- 2. Negative changes in thinking and feeling about oneself
- 3. Negative changes in thinking and feeling about others

Changes in relationships

- 1. Changes in relationships with family and friends
- 2. Changes in relationships with romantic partners
- 3. Changes in relationships with children

Diagnosis: CPTSD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Adjustment Disorder?

Category	Number of symptoms
Re-experiencing trauma (AD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (AD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: AD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Generalized Anxiety Disorder?

Category	Number of symptoms
Re-experiencing trauma (GAD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (GAD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: GAD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Major Depressive Disorder?

Category	Number of symptoms
Re-experiencing trauma (MDD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (MDD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: MDD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Bipolar Disorder?

Category	Number of symptoms
Re-experiencing trauma (BD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (BD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: BD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Schizophrenia?

Category	Number of symptoms
Re-experiencing trauma (S)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (S)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: S is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Borderline Personality Disorder?

Category	Number of symptoms
Re-experiencing trauma (BPD)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (BPD)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

Diagnosis: BPD is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Narcissistic Personality Disorder?

Category	Number of symptoms
Re-experiencing trauma (NP)	1
Avoidance	2
Hyperarousal	3

Re-experiencing trauma (NP)

- 1. Re-experiencing the trauma in the form of flashbacks
- 2. Re-experiencing the trauma in the form of nightmares
- 3. Re-experiencing the trauma in the form of intrusive thoughts

Avoidance

- 1. Avoidance of people, places, or things that remind you of the trauma
- 2. Avoidance of thoughts or feelings about the trauma

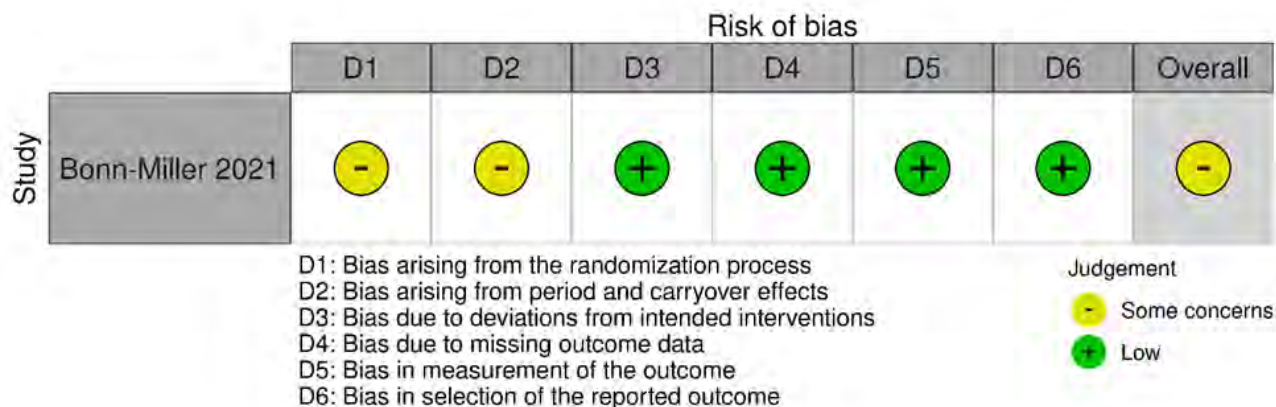
Hyperarousal

- 1. Increased startle response
- 2. Increased irritability
- 3. Increased hypervigilance

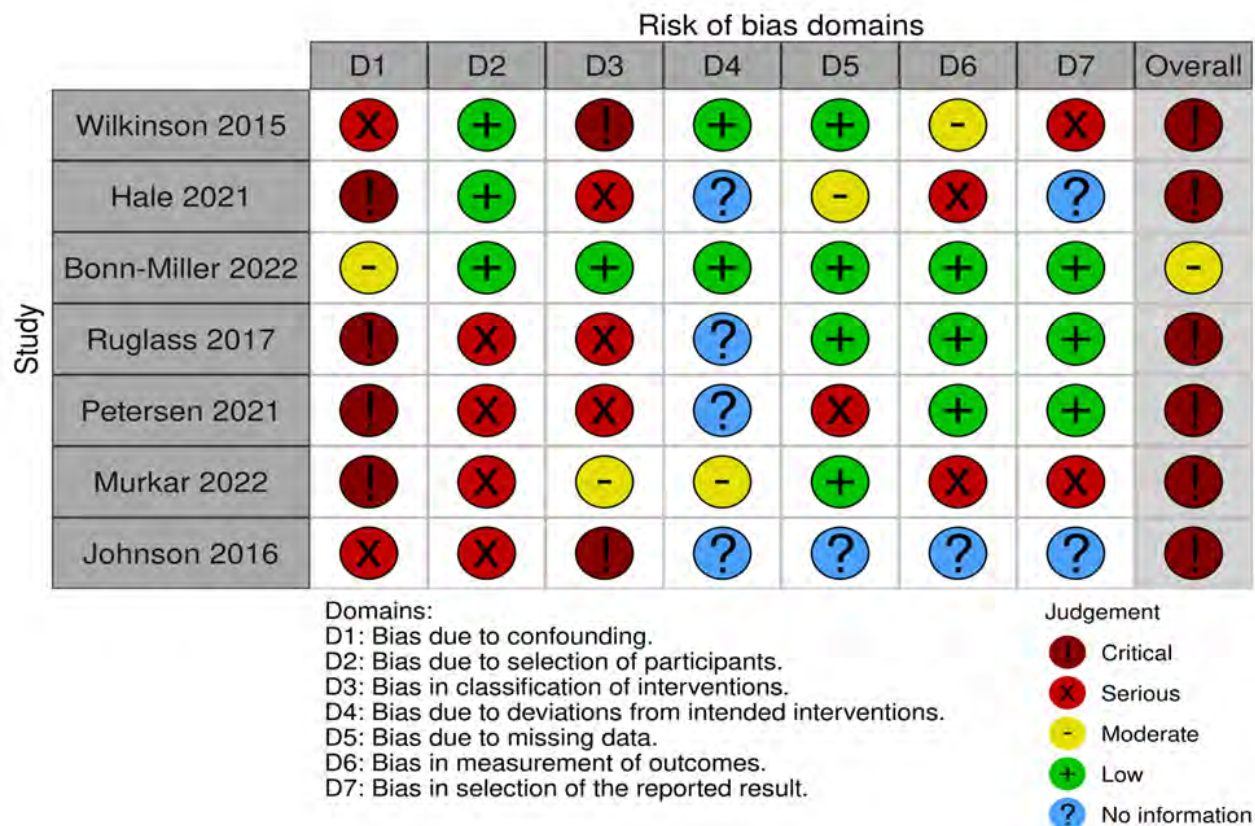
Diagnosis: NP is diagnosed when a person has at least one symptom from each category and the symptoms last for more than one month.

What are the symptoms of Antisocial Personality Disorder?

Category	Number of symptoms
Re-experiencing trauma (AP)	1
Avoidance	2
Hyperarousal	3

Figure 23. Risk of Bias Assessment, Randomized Clinical Trials, Post-Traumatic Stress Disorder

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

Figure 24. Risk of Bias Assessment, Observational Studies, Post-Traumatic Stress Disorder

Source: Consortium for Medical Marijuana Clinical Outcomes Research in Partnership with the Sentinel Initiative. Medical Literature and Data on Marijuana Use. Project 2/1B Report dated July 19, 2023.

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(Slip Opinion)

Questions Related to the Potential Rescheduling of Marijuana

The approach that the Drug Enforcement Administration currently uses to determine whether a drug has a “currently accepted medical use in treatment in the United States” under the Controlled Substances Act is impermissibly narrow. An alternative, two-part inquiry proposed by the Department of Health and Human Services is sufficient to establish that a drug has a “currently accepted medical use” even if the drug would not satisfy DEA’s current approach.

Under 21 U.S.C. § 811(b), a recommendation by HHS that a drug has or lacks a “currently acceptable medical use” does not bind DEA. In contrast, the scientific and medical determinations that underlie HHS’s “currently acceptable medical use” recommendation are binding on DEA, but only until the initiation of formal rulemaking proceedings to schedule a drug. Once DEA initiates a formal rulemaking, HHS’s determinations no longer bind DEA, but DEA must continue to accord HHS’s scientific and medical determinations significant deference, and the CSA does not allow DEA to undertake a *de novo* assessment of HHS’s findings at any point in the process.

Neither the Single Convention on Narcotic Drugs nor the CSA requires marijuana to be placed into Schedule I or II of the CSA. Both the Single Convention and the CSA allow DEA to satisfy the United States’ international obligations by supplementing scheduling decisions with regulatory action, at least in circumstances where there is a modest gap between the Convention’s requirements and the specific restrictions that follow from a drug’s placement on a particular schedule. As a result, DEA may satisfy the United States’ Single Convention obligations by placing marijuana in Schedule III while imposing additional restrictions pursuant to the CSA’s regulatory authorities.

April 11, 2024

MEMORANDUM OPINION FOR THE ATTORNEY GENERAL

The Controlled Substances Act (“CSA”)¹ imposes a unified framework for controlling drugs and other substances that are found to pose a risk of abuse.² In doing so, it seeks to balance several, often competing, interests. These interests include ensuring the availability of drugs that “have a

¹ In 1970, Congress enacted the Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1236, the provisions of which are codified at Chapter 13 of Title 21 of the U.S. Code. The Act comprised several titles, including Title II, which it called the Controlled Substances Act, and Title III, which it called the Controlled Substances Import and Export Act. For ease of reference, we refer to the entire 1970 law as the CSA.

² The CSA applies to both drugs and “other substance[s]” that have been controlled. See 21 U.S.C. § 802(6). For ease of reference, we use the term “drug” to refer to both.

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useful and legitimate medical purpose and are necessary to maintain the health and general welfare of the American people”; preventing the “illegal importation, manufacture, distribution, and possession and improper use of controlled substances [that] have a substantial and detrimental effect on the health and general welfare of the American people”; and ensuring that the United States complies with “international conventions designed to establish effective control over international and domestic traffic in controlled substances.” 21 U.S.C. § 801(1), (2), (7).

The CSA balances these purposes by placing each drug warranting control into one of five “schedules,” with drugs in Schedule I subject to the strictest regulatory and criminal provisions, and drugs in Schedule V subject to the least strict. *See generally* 21 U.S.C. §§ 821–832, 841–865, 951–971. The CSA further authorizes the Attorney General to add, transfer, and remove drugs from the schedules using formal rulemaking procedures, *see id.* §§ 811, 812, and otherwise grants the Attorney General broad authority to take regulatory action consistent with the Act, *see, e.g., id.* §§ 821, 871(b). The Attorney General has in turn generally delegated these functions to the Administrator of the Drug Enforcement Administration (“DEA”). 28 C.F.R. § 0.100(b).

Marijuana has been a Schedule I drug since Congress enacted the CSA. *See* 21 U.S.C. § 812(c). To reschedule marijuana from Schedule I, DEA would need to determine, among other things, that the drug has a “currently accepted medical use in treatment in the United States” (“CAMU”). *Id.* § 812(b). Since 1992, however, DEA has determined that a drug has a CAMU only if either the Food and Drug Administration (“FDA”) has approved the drug for marketing in interstate commerce under the Food, Drug, and Cosmetic Act (“FDCA”), 21 U.S.C. § 301 *et seq.*, or the drug meets a five-part test that tracks the “core standards developed under the FDCA.” 57 Fed. Reg. 10,499, 10,503–04, 10,506 (Mar. 26, 1992). And because FDA has not approved marijuana and DEA has determined that marijuana does not meet its five-part test, DEA has repeatedly rejected petitions to move marijuana to a less restrictive schedule.

On October 6, 2022, President Biden asked the Secretary of Health and Human Services (“Secretary”) and the Attorney General to initiate an “administrative process to review expeditiously how marijuana is scheduled under federal law.” *Statement from President Biden on Marijuana Reform* (Oct. 6, 2022), <https://www.whitehouse.gov/briefing-room/>

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statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform. The CSA requires the Secretary to provide certain recommendations before the initiation of proceedings to schedule or reschedule a drug, and the statute provides that the Secretary's recommendations "shall be binding" as to certain "scientific and medical matters." 21 U.S.C. § 811(b).

Consistent with this requirement, in 2023, the Department of Health and Human Services ("HHS") recommended that DEA reschedule marijuana to Schedule III. *See* Letter for Anne Milgram, Administrator, DEA, from Rachel L. Levine, M.D., Assistant Secretary for Health, HHS (Aug. 29, 2023). HHS concluded that, regardless of whether a drug was approved by FDA or satisfied DEA's five-part test, the drug could have a CAMU if it satisfied a new, two-part inquiry. Part 1 of that inquiry asks whether licensed health care providers have "widespread current experience with medical use" of the drug "in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine." Memorandum for the Commissioner, FDA, from the Assistant Secretary for Health, HHS, *Re: Part 1 Analysis* at 1 (July 17, 2023) ("HHS Part 1 Analysis Memo"). If so, Part 2 of the inquiry asks whether there is "some credible scientific support for at least one of the medical uses." *Id.* at 2.

Against this backdrop, you have asked us three questions:³

- (1) If a drug satisfies the two-part inquiry employed by HHS, does that establish a currently accepted medical use under the statute even if the drug has not been approved by FDA and even if the drug does not satisfy DEA's five-part test?
- (2) To what extent do the "scientific and medical matters" referenced in 21 U.S.C. § 811(b), which are binding upon the Attorney General,

³ This opinion memorializes advice we provided you on February 16, 2024. To aid our analysis, we solicited and received written views from HHS and DEA on all three questions and from the State Department on the third question. *See* Memorandum for the Office of Legal Counsel from DEA (Jan. 30, 2024) ("DEA Response"); Memorandum for Gillian E. Metzger, Deputy Assistant Attorney General, Office of Legal Counsel, from Samuel R. Bagenstos, General Counsel, HHS, *Re: OLC's Request for Views on Issues Related to the Scheduling of Marijuana Under the Controlled Substances Act* (Jan. 29, 2024) ("HHS Response"); Single Convention Requirements for Cannabis and Scheduling Under the Controlled Substances Act (Feb. 12, 2024) ("State Response").

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include the Secretary’s evaluation of a drug’s currently accepted medical use or any scientific and medical considerations involved in that evaluation?

(3) Does the CSA, including the requirement that the Attorney General control drugs “under the schedule he deems most appropriate to carry out” the United States’ “obligations under international treaties, conventions, or protocols in effect on October 27, 1970,” *id.* § 811(d)(1), require DEA to place marijuana in either Schedule I or Schedule II to comply with the Single Convention on Narcotic Drugs, Mar. 30, 1961, 18 U.S.T. 1407 (“Single Convention”)?

As explained in more detail below, we conclude, first, that DEA’s current approach to determining whether a drug has a CAMU is impermissibly narrow, and that satisfying HHS’s two-part inquiry is sufficient to establish that a drug has a CAMU even if the drug has not been approved by FDA and would not satisfy DEA’s five-part test.

Second, we conclude that HHS’s overall CAMU recommendation is not binding on DEA. We also conclude that the scientific and medical determinations that underlie HHS’s CAMU recommendation are binding, but only until the initiation of formal rulemaking proceedings. Once DEA initiates formal rulemaking, HHS’s determinations no longer bind DEA, but DEA must continue to accord HHS’s scientific and medical determinations significant deference, and the CSA does not allow DEA to undertake a *de novo* assessment of HHS’s findings at any point in the process.

Third, we conclude that neither the Single Convention nor the CSA requires DEA to place marijuana in Schedule I or Schedule II. Both the Single Convention and the CSA allow DEA to satisfy the United States’ international obligations by supplementing scheduling decisions with regulatory action, at least in circumstances where there is a modest gap between the Convention’s requirements and the specific controls that follow from a drug’s placement on a particular schedule. As a result, we conclude that DEA may satisfy the United States’ Single Convention obligations by placing marijuana in Schedule III while imposing additional controls pursuant to the CSA’s regulatory authorities.

Questions Related to the Potential Rescheduling of Marijuana

I.

A.

Sections 811 and 812 of the CSA set forth the procedures and standards the Attorney General (and thus DEA) must follow to add a drug to a schedule, transfer a drug between schedules, or remove a drug from the schedules of control. Section 811(a) authorizes the Attorney General to add or transfer a drug to, or remove a drug from, a schedule by issuing a rule “made on the record after opportunity for a hearing” pursuant to the formal rulemaking procedures of the Administrative Procedure Act (“APA”), 5 U.S.C. §§ 553(c), 556, 557. In promulgating such rules, the Attorney General is required to make particular findings, based on substantial evidence, that correspond to the schedule in which the drug is to be placed. 21 U.S.C. §§ 811(a)(1)(A)–(B), 812(b); *see also id.* § 811(b); 5 U.S.C. § 556(d).

Section 812(b) lists the findings the Attorney General must make to place a drug in a particular schedule, with the findings varying by schedule. For example, the Attorney General may place a drug in Schedule I only if the Attorney General finds that the drug “has a high potential for abuse,” 21 U.S.C. § 812(b)(1)(A); “has no currently accepted medical use in treatment in the United States,” *id.* § 812(b)(1)(B); and “[t]here is a lack of accepted safety for use” of the drug “under medical supervision,” *id.* § 812(b)(1)(C). To place drugs in other schedules, the Attorney General must similarly make three findings, except that drugs on the other schedules must have a CAMU (or, in the case of Schedule II drugs, a CAMU with “severe restrictions”). *Id.* § 812(b)(2)(B), (b)(3)(B), (b)(4)(B), (b)(5)(B). Drugs are to be placed in less restrictive schedules as their potential for abuse and likelihood of leading to physiological or physical dependence declines. *Id.* § 812(b)(2)–(5). In the course of making these findings, section 811(c) requires the Attorney General to consider eight medical, scientific, and law-enforcement factors regarding the drug:

- (1) Its actual or relative potential for abuse.
- (2) Scientific evidence of its pharmacological effect, if known.

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- (3) The state of current scientific knowledge regarding the drug or other substance.
- (4) Its history and current pattern of abuse.
- (5) The scope, duration, and significance of abuse.
- (6) What, if any, risk there is to the public health.
- (7) Its psychic or physiological dependence liability.
- (8) Whether the substance is an immediate precursor of a substance already controlled under this subchapter.

Id. § 811(c).

Although section 811 provides that the Attorney General will issue the final rule to schedule a drug, *see id.* § 811(a), the CSA also assigns a significant role in scheduling decisions to the Secretary. Section 811(b) requires the Attorney General, before initiating a rulemaking proceeding to schedule or reschedule a drug, to request both a scientific and medical evaluation of the drug from the Secretary and the Secretary's recommendation as to the schedule, if any, in which the drug should be placed. The Secretary's recommendations "shall be binding on the Attorney General as to such scientific and medical matters" and the Attorney General is prohibited from controlling a drug if the Secretary recommends that it not be controlled. *Id.* § 811(b). After receiving the views of the Secretary, the Attorney General must initiate rulemaking proceedings if there is sufficient evidence to do so. *See id.*

The legislative history of section 811(b) indicates that its purpose was to place scientific and medical judgments in the hands of the Secretary. The report of the House Committee on Interstate and Foreign Commerce explains that "[c]onsiderable controversy arose" during the drafting process over the scheduling provisions of the bill, in particular "with respect to the proper role of the Attorney General and the Secretary of Health, Education, and Welfare [(‘HEW’)]⁴ in making determinations concerning which drugs should be controlled." H.R. Rep. No. 91-1444, at 22 (1970).

⁴ In 1979, Congress created the Department of Education and changed the name of the Department of Health, Education, and Welfare to the Department of Health and Human Services. Department of Education Organization Act, Pub. L. No. 96-88, §§ 201, 509, 93 Stat. 668, 671, 695 (1979).

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This controversy appears to have stemmed from the fact that the version of the CSA that passed the Senate vested full decisionmaking authority regarding scheduling in the Attorney General alone and required only that the Attorney General obtain the “advice” of the Secretary in connection with scheduling decisions. S. 3246, 91st Cong. § 201(a) (1970); *see* 116 Cong. Rec. 1671, 1672 (1970). During the House’s consideration of the bill, Members of Congress, HEW officials, and scientific and medical professionals raised concerns over the dominant role the Senate bill assigned to the Attorney General, arguing that scheduling decisions largely require scientific and medical expertise and that HEW, not the Department of Justice, had this expertise. *See, e.g., Drug Abuse Control Amendments—1970: Hearings Before the Subcomm. on Pub. Health & Welfare of the H. Comm. on Interstate & Foreign Commerce*, 91st Cong. 102–04, 194–95, 199, 550, 557, 580–81 (1970) (“House Hearing”).

Reflecting these concerns, the House version of the bill, H.R. 18583, 91st Cong. (1970), made several changes to what is now 21 U.S.C. § 811(b) that expanded the role of the Secretary and eventually became law. The requirement that the Attorney General obtain “advice” was changed to an obligation to obtain “recommendations” that bound the Attorney General with respect to scientific and medical matters. H.R. 18583, § 201(b). The House bill also added a requirement that the Secretary give a recommendation regarding the schedule in which the drug should be placed and provided that the Attorney General could not control a drug that the Secretary recommended not be controlled. *Id.*

B.

As noted above, Congress classified marijuana as a Schedule I drug when it enacted the CSA in 1970. *See* 21 U.S.C. § 812(c). Shortly thereafter, several organizations petitioned to move marijuana from Schedule I to Schedule V. *See* 37 Fed. Reg. 18,097 (Sept. 7, 1972). The petition was denied three times, but each time on review the United States Court of Appeals for the District of Columbia Circuit remanded for further analysis. *See Nat’l Org. for the Reform of Marijuana Laws v. Ingersoll*, 497 F.2d 654, 661 (D.C. Cir. 1974); *Nat’l Org. for the Reform of Marijuana Laws v. DEA*, 559 F.2d 735, 757 (D.C. Cir. 1977) (“*NORML II*”); *Nat’l Org. for the Reform of Marijuana Laws v. DEA*, No. 79-1660, 1980 U.S. App. LEXIS 13099, at *1 (D.C. Cir. Oct. 16, 1980) (per curiam).

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After the third remand, DEA denied the rescheduling petition once more, concluding that marijuana did not have a CAMU. *See* 54 Fed. Reg. 53,767, 53,767, 53,783–84 (Dec. 29, 1989). In reaching that conclusion, DEA relied on an eight-part test for determining whether a drug had a CAMU that included the following three factors: whether the drug was generally available; whether its use was generally recognized in various medical reference works; and whether its use was recognized by “a substantial segment of the medical practitioners in the United States.” *Id.* at 53,783. As before, the petitioners sought review and the D.C. Circuit remanded the case to DEA, concluding that these three factors were arbitrary and capricious because they would be “logically impossible” for drugs in Schedule I to satisfy. *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 937, 940 (D.C. Cir. 1991) (“*ACT I*”). But the court held that DEA’s interpretation of the statutory phrase “currently accepted medical use” was “in the main acceptable,” and rejected petitioners’ principal argument that DEA’s interpretation unreasonably relied upon “the absence of demonstrated scientific evidence that the drug is medically useful and safe.” *Id.* at 937, 939. In particular, the court noted that the petitioners had presented only “anecdotal evidence” that “a number of physicians believe marijuana is medically useful.” *Id.* at 939.

On remand a fourth time, DEA again denied the petition, again finding that marijuana did not have a CAMU. 57 Fed. Reg. at 10,499. DEA stated that a drug would have a CAMU if it had been approved by FDA under its “New Drug Application” process or if the drug met the criteria to be recognized by FDA as “Generally Recognized As Safe and Effective.” *Id.* at 10,503 (citing 21 U.S.C. §§ 321(p), 355). In addition, DEA concluded that a drug would have a CAMU if it satisfied a new, five-part test (a revised version of DEA’s previous eight-part test that the D.C. Circuit considered in *ACT I*). *Id.* at 10,504. Under DEA’s new test, a drug has a CAMU if the following elements are satisfied:

- (1) the drug’s chemistry is known and reproducible;
- (2) there are adequate safety studies;
- (3) there are adequate and well-controlled studies proving efficacy;
- (4) the drug is accepted by qualified experts; and
- (5) scientific evidence about the drug is widely available.

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Id. at 10,503–06. All five parts were based on the “core FDCA standards for acceptance of drugs for medical use,” and four were expressly derived from the FDCA or FDA regulations setting forth requirements that a drug must meet before receiving FDA approval. *Id.* at 10,504–05 (citing 21 U.S.C. §§ 321(p), (w), 355(d); and 21 C.F.R. §§ 314.103(c)(3), 314.50(d)(1), 314.125(b), 314.126). DEA concluded that marijuana did not meet any of these criteria and accordingly denied the request to remove marijuana from Schedule I. *Id.* at 10,507–08.

This time the D.C. Circuit upheld DEA’s decision. *See All. for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1133 (D.C. Cir. 1994) (“*ACT I*”). It rejected the petitioners’ “central claim” that DEA’s order rested on an “unreasonable interpretation of the statute.” *Id.* The court noted that it had already concluded in *ACT I* that DEA’s interpretation of the CSA was generally reasonable, and it refused to reconsider that determination. *Id.* at 1134. It further reasoned that none of the criteria in DEA’s new five-part test were “impossible for a Schedule I drug to meet” and that DEA had “corrected the flaws [the court] identified in” *ACT I*. *Id.* at 1135.

Since *ACT II*, DEA has denied several petitions that sought rescheduling of marijuana after applying its five-part test and concluding that marijuana did not have a CAMU. *See, e.g.*, 66 Fed. Reg. 20,038, 20,038 (Apr. 18, 2001); 76 Fed. Reg. 40,552, 40,552 (July 8, 2011); 81 Fed. Reg. 53,688, 53,688 (Aug. 12, 2016); 81 Fed. Reg. 53,767, 53,767 (Aug. 12, 2016). Efforts to challenge these denials in court have proven unsuccessful. *See Ams. for Safe Access v. DEA*, 706 F.3d 438, 450 (D.C. Cir. 2013); *Krumm v. DEA*, 739 F. App’x 655 (D.C. Cir. 2018). In recent years, however, several jurists have raised serious concerns about DEA’s conclusion that marijuana does not have a CAMU. *See United States v. Green*, 222 F. Supp. 3d 267, 275 (W.D.N.Y. 2016); *United States v. Amalfi*, 47 F.4th 114, 125 (2d Cir. 2022); *Sisley v. DEA*, 11 F.4th 1029, 1036 (9th Cir. 2021) (Watford, J., concurring).

C.

Since 1996, 38 States, the District of Columbia, and four federal territories have legalized the use of medical marijuana. *See* HHS Part 1 Analysis Memo at 4. These laws typically allow the cultivation, sale, and use of marijuana by patients (or their caregivers) whose health care practitioners have recommended that they use marijuana to treat certain, specified

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conditions. *See, e.g.*, Ohio Rev. Code §§ 3796.01(A)(6)(a)–(v), 3796.08(A); N.Y. Cannabis Law §§ 3(18), 30, 31; N.M. Stat. §§ 26-2B-3(F)(1)–(23), 26-2B-3(N), 26-2B-4(A). Conditions can be added to, or removed from, the list of illnesses that may be treated with marijuana, often by (or at the recommendation of) a state’s public health authorities or special boards convened to consider such matters. *See, e.g.*, Conn. Gen. Stat. § 21a-408l(a), (c); 410 Ill. Comp. Stat. §§ 130/10(h)(2), 130/45; Or. Admin. Rule 333-008-0090. In each fiscal year since 2015, Congress has also adopted an appropriations rider that prohibits the Department of Justice from using funds to prevent certain states, territories, and the District of Columbia from implementing their own laws with respect to medical marijuana. *E.g.*, Consolidated Appropriations Act, 2024, Pub. L. No. 118-42, § 531, 138 Stat. 25; Consolidated Appropriations Act, 2023, Pub. L. No. 117-328, § 531, 136 Stat. 4459, 4561 (2022); *see* Cong. Rsch. Serv., R44782, *The Evolution of Marijuana as a Controlled Substance and the Federal-State Policy Gap* at 26 & n.159 (updated Apr. 7, 2022) (collecting laws).

On October 6, 2022, as noted above, President Biden asked the Secretary and the Attorney General to review how marijuana is scheduled under federal law. As part of its analysis in response to this request, HHS considered whether DEA’s test for determining if a drug has a CAMU was consistent with the text of the CSA. HHS Response at 5–6. HHS agreed that if a drug met the requirements for FDA approval or DEA’s five-part test, the drug would have a CAMU. *Id.* at 8. But it concluded that it would be inconsistent with the text and purpose of the CSA for those standards to be the “sole basis for determining whether a substance has a [CAMU].” *Id.* at 7.

HHS’s analysis instead relied on an additional, two-part inquiry for considering whether a drug has a CAMU. Part 1 of HHS’s inquiry focuses on the extent and nature of medical use. It asks whether there is “widespread current experience with medical use of the substance in the United States by licensed health care practitioners . . . operating in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine.” HHS Part 1 Analysis Memo at 1. HHS further identifies several factors to consider in undertaking this analysis, none being dispositive on its own—specifically, (1) “[w]hether a substantial number of licensed health care practitioners

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have gained clinical experience with at least one specific medical use of the substance under existing and implemented state-authorized programs,” *id.* at 3; (2) “[w]hether a substantial number of entities that regulate the practice of medicine recognize at least one specific medical use of the substance,” *id.*; and (3) “[w]hether licensed health care practitioners’ clinical experience with the medical use of the substance is of sufficient extent and duration to help evaluate potential clinical uses and longer term toxicities and potential harms of the substance when used under medical supervision,” *id.* at 5.

Part 2 of HHS’s test focuses on the scientific basis for any identified medical use. It asks whether there is “some credible scientific support for at least one medical use of the substance for which Part 1 is met.” *Id.* at 2. According to HHS, although again not dispositive, factors that count in favor of the conclusion that some credible scientific support exists include (1) whether “favorable clinical studies of the medical use” of the drug, although not FDA approval-level studies, “have been published in peer-reviewed journals” and (2) whether “[q]ualified expert organizations (e.g., academic or professional societies, government agencies) have opined in favor of the medical use or provided guidance to practitioners on the medical use.” Ctr. for Drug Evaluation & Rsch., FDA, *Considerations for Whether Marijuana Has a Currently Accepted Medical Use in the United States for Purposes of Section 202(b) of the Controlled Substances Act* at 4 (Aug. 28, 2023) (“HHS Part 2 Analysis Memo”). By contrast, factors weighing against the conclusion that such credible scientific support exists include (1) whether “data or information indicates that medical use of the substance poses unacceptably high safety risks for the likely patient population, e.g., due to toxicity concerns”; (2) whether “clinical studies with negative efficacy findings for the medical use have been published in peer reviewed journals”; and (3) whether “qualified expert organizations (e.g., academic or professional societies, government agencies) have recommended against the medical use of the substance.” *Id.* at 4–5.

Applying this two-part inquiry, HHS concluded that marijuana has a CAMU. *Id.* It found that Part 1 of its inquiry was satisfied because more than 30,000 licensed health care practitioners across 43 jurisdictions are authorized to recommend the use of marijuana for more than six million registered patients for at least 15 medical conditions. HHS Part 1 Analysis Memo at 1. HHS also found that Part 2 of its inquiry was satisfied. *See*

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HHS Part 2 Analysis Memo at 7. Although noting that no professional medical organization currently recommends use of marijuana (and that one recommends against its use), HHS concluded after reviewing several studies that there was some credible scientific support that marijuana could be used to effectively treat pain, anorexia, and nausea and vomiting and that using medical marijuana to treat these conditions did not pose “unacceptably high safety risks.” *Id.* at 7. Consistent with this conclusion, and in light of other findings it made, HHS recommended to DEA that marijuana be placed in Schedule III of the CSA.

II.

As discussed above, DEA currently concludes that a drug has a CAMU only if FDA has approved the drug under the FDCA or the drug meets DEA’s five-part test. 57 Fed. Reg. at 10,505–06. HHS agrees with DEA that FDA approval and DEA’s five-part test are sufficient to establish that a drug has a CAMU, *see* HHS Response at 8, and we also agree. To receive FDA approval, a drug must satisfy “rigorous testing and safety reviews” showing that the drug is “both safe and effective.” *Sadoz Inc. v. Becerra*, 57 F.4th 272, 282 (D.C. Cir. 2023). And the entire purpose of FDA’s rigorous approval process is to identify drugs that can be safely and effectively used to treat medical conditions. *See FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133–34 (2000). It would thus make no sense to keep a drug that has met—or could meet—FDA’s standards on Schedule I, which would prevent the drug from being used to treat medical conditions. *See* 21 U.S.C. §§ 829, 841–43.

HHS argues, however, that DEA’s approach to CAMU is impermissibly narrow and that HHS’s two-part inquiry is a permissible way to establish that a drug has a CAMU. You have asked whether, if a drug satisfies the two-part inquiry employed by HHS, that establishes that the drug has a CAMU regardless of whether the drug has been approved by FDA or satisfies DEA’s five-part test. For the reasons that follow, we agree with HHS and conclude that limiting the CAMU analysis to whether a drug has been approved by FDA or meets DEA’s five-part test is an impermissibly narrow interpretation of section 812(b) and that satisfying HHS’s two-part inquiry is sufficient to establish that a drug has a CAMU.

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A.

Section 812(b) requires the Attorney General (and thus DEA), in making scheduling decisions under the CSA, to determine whether a drug has a “currently accepted medical use in treatment in the United States.” It is hard to square DEA’s exclusive reliance on FDA approval and its five-part test with this language.

To begin, DEA’s approach conflicts with the text of section 812(b) by ignoring a wide range of activity that is plainly relevant to whether a drug meets the statutory standard. At the time the CSA was adopted (and as is still true today) the word “accepted” meant “widely used or found” or “generally approved.” *Accepted*, Webster’s Third New International Dictionary 11 (1971); *see also Accepted*, The American Heritage Dictionary of the English Language 8 (1970) (“Generally approved, believed, or recognized.”); *Accepted*, Merriam-Webster.com, <https://www.merriam-webster.com/dictionary/accepted> (last visited Apr. 2, 2024) (defining “accepted” to mean “regarded favorably” or “generally approved or used”). And the focus on “medical use” suggests that the relevant inquiry is whether the medical community has accepted that a drug has a “use in treatment.” 21 U.S.C. § 812(b)(1)(B).

Any examination of whether the medical community “accept[s]” that a drug has a “use in treatment,” *id.*, naturally requires an examination of what licensed health care practitioners are actually doing. Practitioners treat patients, after all, and their treatment decisions and clinical experience with a drug (where such experience exists) provide important evidence in determining whether a medical use is accepted. Moreover, an understanding of what the medical community accepts would also naturally require consideration of the views of the principal regulators of the medical profession: state entities that license and police healthcare practitioners. As the Supreme Court has noted, the CSA “presume[s] and rel[ies] upon a functioning medical profession regulated under the States’ police powers.” *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006).

But neither FDA approval nor DEA’s five-part test examines whether health care practitioners are actually using a drug to treat a condition or whether the entities regulating those practitioners allow the drug to be so used. Instead, FDA approval and DEA’s five-part test rely exclusively on certain scientific evidence and the views of some experts and FDA. Simp-

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ly put, ignoring widespread clinical experience with a drug that is sanctioned by state medical licensing regulators when evaluating whether a drug has a CAMU is at odds with the plain meaning of section 812(b).⁵

Limiting the CAMU analysis to whether a drug has been approved by FDA or meets DEA’s five-part test also conflicts with the text of section 812(b) by erroneously equating identification of an “accepted” medical use under the CSA with the “approval,” or potential approvability, of the drug under the FDCA. Under the CSA, a substance can only be placed on Schedule I if it lacks *both* a “currently accepted medical use in treatment in the United States” *and* an “accepted safety for use . . . under medical supervision.” 21 U.S.C. § 812(b)(1)(B), (C). By contrast, “the FDCA does not even mention the term ‘medical use,’” *Grinspoon v. DEA*, 828 F.2d 881, 887 (1st Cir. 1987), and under the FDCA approval can be denied *either* because the drug is unsafe *or* because it is ineffective, *see* 21 U.S.C. § 355(d)(2), (5). FDA may also deny approval for several other reasons that have nothing to do with medical use, including that the application did not contain the necessary patent information, *see id.* § 355(d)(6), or that the methods used to manufacture, process, and pack the drug “are inadequate to preserve its identity, strength, quality, and purity,” *id.* § 355(d)(3).

Moreover, other CSA provisions confirm that a drug having a CAMU is distinct from it being approved (or approvable) by FDA. Among other things, the CSA elsewhere repeatedly refers to, and in some places explicitly relies on, the FDCA. As an example, 21 U.S.C. § 829 prohibits the dispensing of “prescription drug[s] as determined under the [FDCA]” that are controlled under Schedules II through IV without a prescription from a practitioner, subject to certain exceptions. *See also, e.g., id.* §§ 811(g)(1), 825(e). Congress’s decision to explicitly invoke the FDCA’s standards with respect to some parts of the CSA, but not with respect to whether a drug has a CAMU, strongly suggests that it did not mean to equate CAMU with the standards necessary for FDA approval.

⁵ The First Circuit’s decision in *Grinspoon v. DEA*, 828 F.2d 881 (1st Cir. 1987), is not to the contrary. *Grinspoon* rejected the argument that Congress meant to privilege the views of “certain members of the medical community” in determining if a drug has a CAMU. *Id.* at 892. The court did not consider, however, the broader understanding of the relevant inquiry that we offer here—i.e., whether the medical community as a whole, including practitioners and regulators (among others), has “accepted” that a drug has a “medical use in treatment.” 21 U.S.C. § 812(b)(1)(B).

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Amendments to the CSA reinforce this conclusion. Congress added the “emergency scheduling” provision to the CSA in 1984. Pub. L. No. 98-473, § 508, 98 Stat. 1837, 2071–72 (1984) (codified as amended at 21 U.S.C. § 811(h)). That provision allows the Attorney General to place certain substances in Schedule I on a temporary basis without following the normal scheduling criteria if “necessary to avoid an imminent hazard to the public safety.” 21 U.S.C. § 811(h). But this authority does not apply where an “exemption or approval is in effect for the [drug] under section 505” of the FDCA—i.e., where FDA allows the drug to be marketed in interstate commerce. *See id.*; *see also* Controlled Substances Analogue Enforcement Act of 1986, Pub. L. No. 99-570, tit. I, subtit. E, 100 Stat. 3207, 3207-13 to -14 (codified as amended at 21 U.S.C. § 801(32)) (exempting drugs that have been approved by FDA from the definition of controlled substance analogue). As the First Circuit has observed, these provisions demonstrate that “absolute reliance on the absence of FDA approval” outside of these limited contexts “would be inappropriate and, indeed, contrary to the intent of Congress in enacting the CSA.” *Grinspoon*, 828 F.2d at 890.

We recognize that our conclusion that DEA cannot rely exclusively on FDA approval or its five-part test in determining whether a drug has a CAMU is in some tension with the D.C. Circuit’s decisions in *ACT I* and *ACT II*. The record in those cases, however, was materially different from the one contemplated by HHS’s two-part inquiry: the petitioners in *ACT I* and *ACT II* had shown that, at most, a “number of physicians believe[d] that marijuana is medically useful”—evidence that the court twice said was “anecdotal.” *ACT I*, 930 F.2d at 939; *see also id.* (describing petitioner’s evidence as “largely anecdotal”). Indeed, although the court noted that it “ha[d] no grounds” on the record before it “to dispute [DEA’s] premise that without much more complete scientific data American physicians will not ‘accept’ marijuana,” it further observed that DEA’s conclusion would be “more vulnerable” if “virtually all doctors in the United States were vociferous in their espousal of marijuana for medical treatment—notwithstanding scientific uncertainties.” *Id.*; *see also ACT II*, 15 F.3d at 1134–35 (holding that DEA’s interpretation of “currently accepted medical use” was reasonable on law of the case grounds).

In other words, neither *ACT I* nor *ACT II* assessed DEA’s approach in the circumstance envisioned by HHS’s two-part inquiry—where there is

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“widespread current experience with medical use of” a Schedule I drug in the United States by licensed health care practitioners “operating in accordance with implemented state-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine.” HHS Part 1 Analysis Memo at 1. To the contrary, the D.C. Circuit suggested that such circumstances might never occur, as one of its reasons for rejecting DEA’s original eight-part test was that it “appear[ed] impossible” for a Schedule I drug to meet the requirement that there be “[r]ecognition and use of the [drug] by a substantial segment of the medical practitioners in the United States.” *ACT I*, 930 F.2d at 938, 940. Yet with respect to at least one drug—marijuana—subsequent events have shown that a drug can be in Schedule I but still be recommended for medical use by a large number of medical practitioners in the United States. And for the reasons we have explained, when these circumstances exist, the plain text of section 812 mandates that they be taken into account when determining whether a drug has a CAMU.

B.

Having explained why DEA’s construction of the phrase “currently accepted medical use in treatment in the United States” is impermissibly narrow, we turn to why HHS’s two-part inquiry is sufficient to determine whether a drug has a CAMU.

1.

Part II.A explained that, to determine if a drug has a CAMU, section 812(b) requires an analysis of whether, at the present time, the medical community widely understands that a drug has a “use in treatment in the United States.” Although there is no single right answer as to *how* specifically DEA should make this determination, the text of the CSA establishes certain basic parameters to guide the inquiry.

As an initial matter, the definitions discussed above indicate that “accepted” means that something is “*widely* used or found” or “*generally* approved.” *Accepted*, Webster’s Third New International Dictionary 11 (emphasis added). It therefore follows from the word’s plain meaning that “anecdotal evidence” that a “number of physicians believe that [a drug] is medically useful” is not enough to show that the medical community has

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accepted that a drug has a use in treatment in the United States. *ACT I*, 930 F.2d at 939. At the same time, however, “accepted” does not require universal consensus. Rather, it is sufficient if there is a widespread understanding in the medical community that a drug has a use in treatment.

Relatedly, nothing in the text of the CSA suggests that establishing that a drug has a CAMU requires the medical community to believe that the drug is the best way to treat a condition. So long as there is widespread understanding in the medical community that a drug is a permissible and reasonable way to treat a condition, it has a CAMU. That reflects a basic reality about the medical profession: that “in medicine there is often a range of reasonable treatments[.]” *Young v. United States*, 942 F.3d 349, 352 (7th Cir. 2019).

Moreover, the medical community is not a monolith: It contains individuals and entities with a range of expertise and experiences, including licensed health care practitioners who specialize in certain areas of medicine, generalists with broader expertise, researchers, and regulators. In assessing the views of the medical community, section 812(b)(1)(B)’s emphasis on a “medical use in treatment” indicates that the views of all these constituencies are not equally important in every case. Instead, to determine whether the medical community understands using a particular drug to be within the range of reasonable treatment options, it is the views and practices of the health care practitioners who actually treat a given condition, as well as the regulators charged with enforcing applicable norms of practice, that are often especially relevant.

Finally, we believe a CAMU test must include consideration of the scientific evidence that supports the relevant medical use. This follows from section 811(c)’s requirement that the Attorney General “shall consider” eight factors in making the CAMU determination and other findings under section 812(b), some number of which inherently require consideration of scientific evidence. Although it is unclear exactly how the eight factors listed in section 811(c) correlate to the findings required by section 812(b), it is plain that at least two of those factors—the “scientific evidence of [the drug’s] pharmacological effect, if known” and the “state of current scientific knowledge regarding the drug,” 21 U.S.C. § 811(c)(2), (3)—bear on whether a drug has a currently accepted medical use, and that those factors necessarily require evaluation of scientific evidence. In addition, the requirement to consider “[w]hat, if any, risk there is to the

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public health” and the drug’s “psychic or physiological dependence liability,” *id.* § 811(c)(6), (7), further suggests that an assessment of the available science is an integral part of a CAMU determination. Reviewing the available scientific evidence as part of the CAMU analysis is also consistent with the common-sense intuition that there is an inherent connection between whether the medical community has “accepted” a drug for “use in treatment,” *id.* § 812(b)(1)(B), and the scientific evidence supporting that conclusion. We generally would not expect the medical community to understand that it is reasonable to use a drug to treat a condition unless (as HHS suggests) there is at least some scientific evidence in support of that conclusion—evidence demonstrating, for example, that the drug was effective in treating the condition or does not create unacceptably high safety risks. HHS Part 2 Analysis Memo at 4–5.

2.

We conclude that HHS’s two-part inquiry falls within the basic parameters the CSA provides for establishing that a drug has a CAMU.

Part 1 of HHS’s test requires an assessment of whether health care practitioners are recommending that patients use a drug to treat a medical condition and whether they are doing so in accordance with guidelines issued by entities that regulate the practice of medicine. This approach is consistent with our view that determining whether a drug has a CAMU requires assessing whether there is a widespread understanding in the medical community that using the drug to treat a condition falls within the range of reasonable treatment options. In particular, the actual recommendations of practitioners made under applicable regulatory guidelines constitute strong evidence of whether the medical community understands a drug to be a reasonable treatment option.

The three non-dispositive factors HHS includes in its Part 1 analysis further demonstrate why its test is sufficient. Two of HHS’s factors look, respectively, at whether a “substantial number of licensed health care practitioners” have gained clinical experience with a drug under a state-authorized program and whether a “substantial number” of entities that regulate the practice of medicine have authorized the use of a drug for medical purposes. *See* HHS Part 1 Analysis Memo at 3. In our view, these inquiries provide good evidence of whether there is widespread agreement within the medical community that using the drug would be a reasonable

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treatment option. Similarly, it is more likely that the medical community would widely understand that a drug represents a reasonable treatment option if HHS's third factor is present—i.e., that practitioners' clinical experience with the drug is of a "sufficient extent and duration" to help evaluate whether there are "potential clinical uses," "longer-term toxicities," and "potential harms." *Id.* at 5.

Moreover, Part 2 of HHS's test adequately takes the available scientific evidence into account by asking whether there is some credible scientific support for a least one of the medical uses for which the Part 1 test is met and then providing guidance as to what counts as "credible" scientific support. *See* HHS Part 2 Analysis Memo at 4 (identifying "favorable clinical studies" published in peer-reviewed journals as cutting in favor of the conclusion that the drug has a CAMU); *id.* (identifying data or information that "indicate[s] that medical use of the [drug] is associated with unacceptably high safety risks for the likely patient population" because of "toxicity concerns" as cutting against the conclusion that the drug has a CAMU). Neither section 811(c) nor section 812(b) requires a particular threshold of scientific support to conclude that a drug has a CAMU, and we believe that Part 2's requirement of some credible scientific support is sufficient in a context where health care practitioners have extensive experience with a drug and medical regulators have sanctioned the drug's use. Such clinical experience and regulatory sanction provide alternative sources of information about a drug, thereby making it reasonable not to require the high level of scientific support that might be demanded before a new and untried drug is determined to have a CAMU.

DEA's main concern with HHS's two-part inquiry is that it places too much emphasis on state regulatory decisions. Specifically, DEA suggests that HHS's emphasis on states is "misplaced" because, in DEA's view, the processes states follow for enacting legislation "are generally less rigorous than the requirements placed on federal agencies when they act pursuant to the APA." DEA Response at 11. But there is nothing in the text of the CSA that would warrant categorically discounting state practice in this fashion, particularly since doing so would be inconsistent with both the role of states as the central regulators of medical practice, *see Oregon*, 546 U.S. at 270, 274–75, and the fact that they are afforded "great leeway" in adopting measures to "protect public health and safety," *Mackey v. Montrym*, 443 U.S. 1, 17 (1979). Indeed, Congress has already

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recognized the importance of states' views on whether marijuana in particular may be used to treat medical conditions by annually adopting an appropriations rider that prohibits the Department of Justice from using funds to prevent certain states, territories, and the District of Columbia from implementing their own laws with respect to medical marijuana. *See supra* Part I.C.

In addition, states do often look to scientific and medical judgment in regulating medical marijuana. States typically only allow medical practitioners to recommend medical marijuana to treat specific conditions. *See, e.g.*, Ohio Rev. Code § 3796.01(A)(6)(a)–(v); N.Y. Cannabis Law § 3(18). In some states, practitioners may only recommend the use of medical marijuana after determining that the patient suffers from one of those conditions and that the “potential benefits of the palliative use of marijuana would likely outweigh the health risks of such use.” *E.g.*, Conn. Gen. Stat. § 21a-408c(a); *see also* Fla. Stat. § 381.986(4). Several states have also established processes through which experts can recommend additions to, or removals from, the list of conditions that marijuana may be used to treat, *see, e.g.*, Conn. Gen. Stat. § 21a-408l(a), (c)(1), (d); Or. Admin. Rule 333-008-0090(3)(e), (4)(a)—indeed, HHS has informed us that 17 jurisdictions have added conditions that may be treated with marijuana using such processes, *see* HHS Part 1 Analysis Memo at 4. In short, it is simply not the case that state practice concerning medical marijuana is completely divorced from scientific and medical assessment.

III.

As discussed above, the CSA authorizes the Attorney General to place drugs in particular schedules if, after a formal rulemaking, the Attorney General makes certain findings. A particularly important finding is whether a drug has a CAMU, as the Attorney General may only keep or place a drug in Schedule I if it lacks a CAMU. Before initiating a rulemaking proceeding to schedule or reschedule a drug, however, the Attorney General is required to request recommendations from the Secretary that must include whether the drug has a CAMU. *See* 21 U.S.C. § 811(b). The CSA further makes these recommendations binding “as to” certain “scientific and medical matters.” *Id.*

Since HHS has recommended that marijuana has a CAMU, you have asked about the extent to which the “scientific and medical matters” that

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are binding on the Attorney General, and thus DEA, include HHS's CAMU recommendation or any scientific and medical determinations underlying that recommendation. For the reasons that follow, we conclude, first, that HHS's overall CAMU recommendation is not binding on DEA. Second, we conclude that the scientific and medical determinations that underlie HHS's CAMU recommendation are binding, but only until the initiation of formal rulemaking proceedings. Once DEA initiates formal rulemaking, HHS's determinations no longer bind DEA, but DEA must continue to accord HHS's scientific and medical determinations significant deference, and the CSA does not allow DEA to undertake a *de novo* assessment of HHS's findings at any point in the process.

A.

We first explain why HHS's overall CAMU recommendation does not bind DEA, starting with the two CSA provisions that govern the CAMU determination. Section 811(a) authorizes the Attorney General to schedule or reschedule a drug if the Attorney General makes certain findings "on the record after opportunity for a hearing pursuant to the rulemaking procedures prescribed by [the APA]." Section 812(b) then lays out the relevant findings the Attorney General must make to schedule a drug, including whether the drug has a CAMU.

Taken together, these two provisions commit exclusively to the Attorney General the ultimate responsibility for making the findings required to schedule a drug, including a CAMU finding, and neither mentions the Secretary at all. Instead, the role of the Secretary is addressed in a separate provision of the CSA, section 811(b), which reads as follows:

The Attorney General shall, before initiating proceedings under subsection (a) to control a drug or other substance or to remove a drug or other substance entirely from the schedules, and after gathering the necessary data, request from the Secretary a scientific and medical evaluation, and his recommendations, as to whether such drug or other substance should be so controlled or removed as a controlled substance. In making such evaluation and recommendations, the Secretary shall consider the factors listed in paragraphs (2), (3), (6), (7), and (8) of subsection (c) and any scientific or medical considerations involved in paragraphs (1), (4), and (5) of such subsection. The

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recommendations of the Secretary shall include recommendations with respect to the appropriate schedule, if any, under which such drug or other substance should be listed. The evaluation and the recommendations of the Secretary shall be made in writing and submitted to the Attorney General within a reasonable time. The recommendations of the Secretary to the Attorney General shall be binding on the Attorney General as to such scientific and medical matters, and if the Secretary recommends that a drug or other substance not be controlled, the Attorney General shall not control the drug or other substance. If the Attorney General determines that these facts and all other relevant data constitute substantial evidence of potential for abuse such as to warrant control or substantial evidence that the drug or other substance should be removed entirely from the schedules, he shall initiate proceedings for control or removal, as the case may be, under subsection (a).

This provision makes clear that the Secretary plays a crucial role in the scheduling process. It expressly directs the Attorney General to obtain a scheduling recommendation from the Secretary before initiating the scheduling process and to treat as binding certain “scientific or medical matters.” *Id.*⁶ But section 811(b) does not so much as mention the Secretary’s

⁶ In two recent rulemakings, DEA has stated that HHS’s scientific and medical recommendations only bind DEA with respect to factors (1), (4), and (5) of section 811(c). See 86 Fed. Reg. 29,506, 29,507–08 (June 2, 2021); 86 Fed. Reg. 27,803, 27,805 (May 24, 2021). This view appears to be based on a contrast in section 811(b)’s text: it directs the Secretary to “consider the factors listed in paragraphs (2), (3), (6), (7), and (8) of [section 811(c)],” and “any scientific or medical considerations involved in paragraphs (1), (4), and (5) of [section 811(c)],” with the Secretary’s recommendations being “binding . . . as to such scientific and medical matters.” But section 811(b) highlights the “scientific and medical considerations” in factors (1), (4), and (5) not because HHS should consider the science and medicine underlying only those factors, but rather because those factors all relate to a drug’s abuse potential, the analysis of which Congress understood as resting primarily on law enforcement considerations. See H.R. Rep. No. 91-1444, at 33–36; House Hearing at 718. By comparison, there is no need to direct HHS to consider the “scientific or medical considerations” involved with factors (2), (3), (6), (7), and (8) since those factors involve inquiries that are predominantly, if not entirely, scientific and medical in nature. We thus think it plain that HHS’s recommendations with respect to “scientific and medical matters” are binding for all eight factors listed in section 811(c). See H.R. Rep. 91-1444, at 33; see also *id.* at 22–23 (“[A]ll scientific and

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CAMU recommendation. Instead, section 811(b) expressly identifies a different circumstance in which the Secretary’s recommendation concerning an ultimate scheduling determination is dispositive: when the Secretary recommends against controlling a drug. This fact—that section 811(b) identifies a separate scheduling recommendation as binding—makes its silence on the Secretary’s CAMU recommendation all the more conspicuous.

Moreover, we do not believe the Secretary’s authority to bind the Attorney General with respect to “scientific and medical matters” encompasses a CAMU determination, because such a determination involves judgments that are neither wholly scientific nor wholly medical. For example, as the discussion in Part II indicates, assessing whether a drug has a CAMU may involve, in part, determining whether the extent of medical use present is sufficient to qualify as “accepted” within the medical community. 21 U.S.C. § 812(b)(1)(B). This inquiry is more akin to the application of a legal standard to a set of facts than a judgment necessarily requiring medical or scientific expertise, as it could turn (at least in part) on reasoning or facts that are neither scientific nor medical in nature, such as determining how many states have authorized use of a drug in treating a medical condition. *Cf., e.g., United States v. Garcia*, 413 F.3d 201, 215 (2d Cir. 2005) (conclusions that are the “product of reasoning processes familiar to the average person in everyday life” do not require specialized expertise); *accord United States v. Vega*, 813 F.3d 386, 394–95 (1st Cir. 2016) (conclusions based on “logic and pattern recognition” do not require specialized expertise). Because a CAMU determination can include elements that fall outside the substantive scope of HHS’s authority to bind DEA, HHS’s overall determination that a substance has (or lacks) a CAMU cannot be binding.

B.

We next explain why the scientific and medical determinations underlying HHS’s overall CAMU recommendations bind DEA, although only until the initiation of formal rulemaking, and why DEA is nonetheless obligated to accord the findings significant deference thereafter.

medical determinations [will be] made by the Secretary of Health, Education, and Welfare[.]” (emphasis added)).

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As a threshold matter, the text and legislative history of section 811(b) demonstrate that the “scientific and medical matters” binding on the Attorney General include the scientific and medical determinations that underlie the Secretary’s CAMU recommendation. *See* H.R. Rep. No. 91-1444, at 33; HHS Response at 10; DEA Response at 16. For example, whether some credible scientific support exists for a particular widespread clinical use, *see supra* Part I.C, is undoubtedly relevant to a CAMU finding—and undoubtedly a “scientific and medical matter.”

The more difficult question, however, is whether HHS’s scientific and medical determinations remain binding throughout the scheduling process—a question on which DEA and HHS hold sharply different views. DEA argues that it “is only bound by HHS’s evaluation as to scientific and medical matters . . . at the beginning of the [scheduling] process,” but “[o]nce rulemaking has begun, DEA can—and must—consider material submitted during the administrative process in reaching a final scheduling determination.” DEA Response at 13; *see also* 76 Fed. Reg. 77,330, 77,334–36 (Dec. 12, 2011) (adopting this position). HHS takes the opposite view, arguing that its scientific and medical recommendations bind DEA throughout the scheduling process, including the formal rulemaking. *See* HHS Response at 10–11.

The CSA is unquestionably hard to parse on this issue. It does not expressly address for what portion of the administrative proceedings HHS’s determinations are binding, nor does it specify how, if at all, such determinations must be considered during the formal rulemaking proceedings. Moreover, what clues the statute does offer point in two opposing directions: On the one hand, the statute requires the Attorney General alone to make the ultimate findings required for scheduling after an on-the-record formal rulemaking, which implies that the Attorney General must consider contrary scientific or medical evidence submitted during that process. *See* 21 U.S.C. § 811(a). On the other hand, the statute makes the Secretary’s scientific and medical determinations “binding” on the Attorney General without expressly limiting the binding nature of those determinations to any particular stage of the scheduling process. *See id.* § 811(b).

Although a close question, we think Congress’s decision to make scheduling decisions subject to a formal rulemaking process ultimately provides the answer. Fundamentally, the proposition that HHS’s determinations bind DEA for the entirety of the scheduling process cannot be

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squared with the nature of the formal rulemaking that section 811(a) requires. Nothing in the CSA limits outside participants to submitting only nonscientific and nonmedical evidence at a rulemaking hearing. Given the possibility that parties may submit contrary scientific or medical evidence, construing section 811(b) to preclude DEA from considering such evidence would be inconsistent with the APA's requirement that rules issued via formal rulemaking be based "on consideration of the whole record . . . and supported by and in accordance with the reliable, probative, and substantial evidence." 5 U.S.C. § 556(d); *see Universal Camera Corp. v. NLRB*, 340 U.S. 474, 488 (1951) ("The substantiality of evidence must take into account whatever in the record fairly detracts from its weight. This is clearly the significance of the requirement . . . [to] consider the whole record."). In short, DEA would not be making a decision based on the "whole record" and "in accordance with the reliable, probative, and substantial evidence," 5 U.S.C. § 556(d), if HHS's determinations barred DEA from considering contrary scientific or medical evidence. Two courts of appeals have suggested in dicta that they view the issue similarly. *See Grinspoon*, 828 F.2d at 890; *Reckitt & Colman, Ltd. v. Administrator, DEA*, 788 F.2d 22, 27 n.8 (D.C. Cir. 1986).

The fact that HHS's recommendations as to certain "scientific and medical matters" do not bind DEA for the entire scheduling process does not mean, however, that they are without effect. Rather, in order to give force to the statutory command that HHS's recommendations "bind[]" DEA, we believe HHS's scientific and medical determinations must be binding until the issuance of a notice of proposed rulemaking ("NPRM"). Up to this point, the formal rulemaking procedures required by section 811(a) are not yet in effect, *see* 21 C.F.R. §§ 1308.43(f), 1316.42(g), meaning there is no conflict between the statutory commands to consider contrary evidence in the record and accord binding effect to HHS's recommendations.

In addition, DEA may not simply cast aside HHS's scientific and medical recommendations once it initiates formal rulemaking proceedings by issuing an NPRM. The categorical use of the word "binding" in section 811(b) suggests that Congress intended HHS's scientific and medical views to at least be a very significant input in the scheduling process. And there would seem to be little reason to make the HHS's views binding at any stage in the process if DEA eventually could discard HHS's determi-

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nations and review scientific and medical matters *de novo*. *Cf. Reno v. Am.-Arab Anti-Discrimination Comm.*, 525 U.S. 471, 487 (1999) (statutes should be read in a manner that “makes sense of the statutory scheme as a whole”).

The legislative history of the CSA supports the view that HHS’s scientific and medical determinations should remain significant throughout the rulemaking process. The House report on the CSA states that Congress intended “all scientific and medical determinations” to be “made by the Secretary,” rather than the Attorney General, and nothing in the legislative history suggests that the Attorney General would be free to make *de novo* scientific and medical judgments once the formal rulemaking is underway. H.R. Rep. No. 91-1444, at 22–23. Indeed, the House report emphasized that section 811 was “not intended to authorize the Attorney General to undertake or support medical and scientific research” for the purpose of scheduling, as that research “is within the competence of [HHS].” *Id.* at 33. And considering this same legislative history, the Supreme Court noted in *Gonzales* that the CSA places “medical judgments” made under the Act in the “hands of the Secretary.” 546 U.S. at 265.

We therefore conclude that, to give proper effect to HHS’s scientific and medical determinations, DEA must continue to accord significant deference to those determinations even once formal rulemaking has commenced and may not undertake a *de novo* assessment of HHS’s findings at any point in the rulemaking process.

IV.

The Single Convention requires parties to impose controls on the cultivation, manufacture, and distribution of various drugs, including “cannabis.”⁷ Among other things, parties to the Convention generally must

⁷ The Convention defines “cannabis” as “the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted, by whatever name they may be designated.” Single Convention art. 1(1)(b). We understand the marijuana in use in the United States to fall within this definition, although the definition of cannabis under the Single Convention is slightly less inclusive than the CSA’s definition of “marihuana,” which includes all parts of the *Cannabis sativa* L. plant with certain exceptions, including mature stalks and sterilized seeds that are incapable of germination. *See* 21 U.S.C. § 802(16).

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require that manufacturers, distributors, importers, and exporters of cannabis secure a license, Single Convention arts. 29–31; impose quotas on the import and manufacture of cannabis, *id.* art. 21(1); generally prohibit the unauthorized possession of cannabis, *id.* art. 33; and adopt penal provisions making violations of the controls required by the Convention punishable offenses, *id.* art. 36.

Several provisions of the CSA—including sections 801(7), 811(d)(1), 812(b), 823(a), 953(a), and 958(a)—“reflect Congress’s intent to comply with the obligations imposed by the Single Convention.” *Control of Papaver bracteatum*, 1 Op. O.L.C. 93, 95 (1977). Of particular relevance here, section 811(d)(1) provides:

If control is required by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings required by subsection (a) of this section or section 812(b) of this title and without regard to the procedures described by subsections (a) and (b) of this section.

The Single Convention entered into force for the United States on June 24, 1967, and was thus “in effect on October 27, 1970.” *Id.* Both our Office and the D.C. Circuit have interpreted section 811(d)(1) to apply to any scheduling action by the Attorney General concerning a drug covered by the Single Convention, including actions to transfer a drug between schedules. Memorandum for John E. Ingersoll, Director, Bureau of Narcotics & Dangerous Drugs, from Mary C. Lawton, Deputy Assistant Attorney General, Office of Legal Counsel, *Re: Petition to Decontrol Marihuana; Interpretation of Section 201 of the Controlled Substances Act of 1970* at 9 (Aug. 21, 1972) (“Lawton Memo”); *NORML II*, 559 F.2d at 747.

Given this, your third question asks whether the CSA or the Single Convention requires marijuana to be placed in Schedule I or Schedule II. This question is one our Office has considered before: in 1972, we concluded that the Convention requires marijuana to be placed in Schedule I or II because placing marijuana in Schedules III, IV, or V would not enable the United States to satisfy its Convention obligations. *See* Lawton Memo at 12–13. In particular, we emphasized that the “quotas on manu-

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facture and importation of a substance required by the Convention could not be maintained under existing statutory authority were marihuana listed in Schedules III, IV, or V.” *Id.*; see also *NORML II*, 559 F.2d at 750–51 (agreeing with the Lawton Memo that Schedule I or II was necessary to meet the United States’ Single Convention obligations). In reaching this conclusion, however, we did not address an issue that both HHS and the State Department now ask us to consider: whether under the CSA the United States can comply with its Single Convention obligations by placing marijuana in Schedule III while “adopting such additional regulations as are necessary for treaty compliance.” HHS Response at 13; State Response at 5–7; see also *NORML II*, 559 F.2d at 752–53 (recognizing the possibility of a similar regulatory approach but taking no position on its availability).

We think this question is a close one. For the reasons that follow, however, we believe that the Single Convention does not require DEA to place marijuana in Schedule I or Schedule II. Both the Single Convention and the CSA allow DEA to satisfy the United States’ international obligations by supplementing scheduling decisions with regulatory action, at least in circumstances where there is a modest gap between the Convention’s requirements and the specific controls that follow from a drug’s placement on a particular schedule. And consistent with this conclusion, we believe DEA may satisfy the United States’ Single Convention obligations by placing marijuana in Schedule III while imposing additional controls pursuant to the CSA’s regulatory authorities.

A.

To begin, nothing in the Single Convention requires the United States to comply with its international obligations by placing a drug in a statutory “schedule” that specifically authorizes all the necessary restrictions. To the contrary, the Single Convention states that parties will implement the Convention using both “laws and *regulations*.” Single Convention art. 18(1)(b) (emphasis added); see also *id.* art. 4 (referring to the use of “legislative and *administrative measures*” to carry out the Single Convention (emphasis added)). The Single Convention thus appears to explicitly contemplate a scenario in which DEA decides to implement the United States’ obligations through a combination of scheduling and regulatory actions.

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As a result, any limitation on satisfying the United States’ Single Convention obligations by supplementing a scheduling decision with regulatory action would have to come from domestic law. Nothing in the CSA, however, states that a drug must be placed into Schedule I or II, or any other particular schedule, to comply with the Single Convention. Nor does the CSA expressly foreclose DEA from satisfying the United States’ international obligations with a combination of scheduling and regulatory actions. Rather, section 811(d)(1) directs the Attorney General to “control[]” a drug “under the schedule [the Attorney General] *deems most appropriate*” (emphasis added)—language that signals a broad grant of discretion to the Attorney General (and thus DEA), *see Rex Chainbelt, Inc. v. Volpe*, 486 F.2d 757, 761 (7th Cir. 1973). To be sure, the very same language could be read to mean that DEA must select a schedule without resort to regulatory supplementation. *See* 21 U.S.C. § 802(5) (defining “control” as “to add a drug . . . to a *schedule*” (emphasis added)). But we are reluctant to adopt a restrictive reading of such broad discretionary language, particularly when doing so would preclude DEA from relying on regulatory supplementation to close even relatively minor gaps between a schedule and the United States’ international obligations. Indeed, consistent with this reading, DEA has previously placed a drug with the psychoactive chemicals found in cannabis into Schedule V and then imposed additional controls through regulation to comply with the United States’ international obligations. *See* 83 Fed. Reg. 48,950, 48,952 (Sept. 28, 2018).⁸

The CSA’s varied, and potentially conflicting, purposes further show why it is appropriate to read section 811(d)(1)’s broad grant of authority in this way. Consider a hypothetical case in which the Single Convention imposes obligations that DEA determines would, absent regulatory action,

⁸ We have taken a similar interpretive approach to section 811(d)(1)’s language specifying that the Attorney General meet international obligations “without regard” to the findings and procedures otherwise required by sections 811(a) through (b) and 812(b). Rather than viewing this language as precluding the Attorney General from following ordinary scheduling practices when international obligations are involved, both our Office and the D.C. Circuit have understood it to allow the Attorney General to identify which schedules would satisfy the United States’ international obligations with respect to a particular drug, and then—if more than one schedule would do so—select which schedule to use through the section 811(a) through (b) and 812(b) procedures. Lawton Memo at 10; *accord NORML II*, 559 F.2d at 747.

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require placement on Schedule I or Schedule II, but DEA has also determined that the same drug’s abuse potential, medical usefulness, and health effects warrant placing the drug in Schedule III. *See* 21 U.S.C. §§ 801(1), (2), 812(b)(3). In such a circumstance, reading section 811(d)(1) to allow for consideration of regulatory action allows DEA to conclude that Schedule III is the “most appropriate” schedule by pairing that choice with regulatory actions that ensure compliance with the Single Convention. This enables DEA to comply with the United States’ international obligations while furthering the CSA’s other purposes, thus fulfilling both sets of objectives.

The broad regulatory authority provided by the CSA further suggests that DEA need not rely on scheduling decisions alone to comply with the Single Convention. The CSA authorizes the Attorney General (and thus DEA) both to “promulgate rules and regulations . . . relating to the registration and control of the manufacture, distribution, and dispensing of controlled substances,” *id.* § 821, and to “promulgate and enforce any rules, regulations, and procedures which he may deem necessary and appropriate for the efficient execution of his functions,” *id.* § 871(b). Courts recognize that broad, discretionary language such as this conveys “extensive” regulatory authority, *Volpe*, 486 F.2d at 761; *see also, e.g., Friends of Animals v. Bernhardt*, 961 F.3d 1197, 1209 (D.C. Cir. 2020)—and, here, the language by its plain terms would seem to encompass regulatory actions that DEA may take to satisfy Single Convention obligations not met by a drug’s schedule alone.

Likewise, the CSA provides the Attorney General with a number of more specific regulatory authorities that DEA may use to enable compliance with particular Single Convention obligations, such as the CSA’s registration requirements. Subject to certain limited exceptions, section 822(a) requires “[e]very person who manufactures or distributes” or “dispenses” a drug to “obtain annually a registration issued by the Attorney General in accordance with rules and regulations promulgated by him,” and section 822(b) further specifies that “[p]ersons registered by the Attorney General under this subchapter to manufacture, distribute, or dispense controlled substances . . . are authorized to possess, manufacture, distribute, or dispense such substances . . . to the extent authorized by their registration.” These provisions give DEA the authority to impose a number of controls on a particular drug through registration. Other CSA

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provisions provide similar regulatory authority that could enable a drug on a schedule other than Schedule I or Schedule II to comply with the Single Convention. *See, e.g.*, 21 U.S.C. §§ 823(e), (f), 827(e), 952(b)(2), 953(e)(2), 958(c).

Finally, past practice also supports our conclusion. Specifically, in addition to the example recounted above of DEA imposing additional controls through regulation to comply with the United States' international obligations, *see* 83 Fed. Reg. at 48,952, we understand that DEA previously has relied on a combination of the Attorney General's registration power and general regulatory authority to promulgate extensive safety and security regulations that govern manufacturers and distributors of controlled substances. *See* 21 C.F.R. §§ 1301.71–.77. And our Office has previously read the Attorney General's authority to register manufacturers broadly to permit the imposition of certain controls that would enable compliance with the Single Convention. *See Licensing Marijuana Cultivation in Compliance with the Single Convention on Narcotic Drugs*, 42 Op. O.L.C. __, at *24 (June 6, 2018) ("*Licensing Marijuana Cultivation*"). These prior regulatory actions indicate that the broad and varied provisions discussed above provide authority that may be used to impose additional controls to satisfy the United States' international obligations.

We recognize that reading the CSA as allowing DEA to use regulatory authorities to close gaps in our compliance with international obligations could be viewed as in tension with certain aspects of the CSA's text and structure. As the Lawton Memo noted, several provisions of the CSA implementing controls required by the Single Convention draw a distinction between Schedules I and II, on the one hand, and Schedules III through V, on the other, in a manner that can be read to suggest that Congress understood the United States would comply with its Convention obligations by placing drugs into Schedules I or II. Lawton Memo at 12; *see, e.g.*, 21 U.S.C. §§ 823(a), (d), (e), 826(a), 842(b), 952(a), (b), 958(a), (c). Moreover, Congress designed the CSA to include five schedules, each with a distinct bundle of requirements and consequences, and allowing DEA to add or subtract controls would arguably have the practical effect of enabling DEA to create new schedules.

These arguments have some force, but they do not carry the day. Since the CSA's enactment, Congress has amended the Act in a manner that indicates the distinction between Schedules I and II and Schedules III

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through V may not be as sharp as the argument above suggests. *See infra* Part IV.B (describing how amendments that added sections 952(b)(2), 953(e)(2), and 827(e) enable the United States to meet certain Single Convention obligations while placing nonnarcotic drugs in Schedule III). In any event, right alongside the provisions that could *impliedly* suggest Schedules I and II will be used to comply with the United States’ Single Convention obligations are provisions that *expressly* grant the Attorney General (and thus DEA) both broad discretion to select the schedule “most appropriate” to satisfy the United States’ international obligations, *see* 21 U.S.C. § 811(d)(1), and broad regulatory authority, *see, e.g., id.* §§ 821, 871(b). And given the plain meaning of the CSA’s regulatory provisions, we do not believe that the CSA’s five-schedule structure can be reasonably understood to preclude DEA from taking at least some regulatory actions to comply with the United States’ international obligations. Indeed, it would be particularly strange to view DEA as so constrained in the context of treaty compliance, given section 811(d)(1)’s express grant of broad discretion to meet international obligations. We therefore believe that something more than such textual and structural inferences are needed to foreclose use of these broad and express statutory grants of regulatory authority to impose additional controls to meet the United States’ international obligations.

Thus, while we take no position on the full extent to which DEA may use the CSA’s broad regulatory authority to impose additional controls to meet international obligations, we do not read the CSA as precluding DEA from ever satisfying the United States’ Single Convention obligations by supplementing scheduling decisions with regulatory action. Rather, we believe that the CSA provides DEA with the discretion to decide, at least in some circumstances, that such a scheduling and regulatory approach is the most appropriate way to strike a balance between the CSA’s varied—and potentially conflicting—purposes of curtailing the improper use of drugs with abuse potential, complying with the United States’ international obligations, and ensuring that medically useful drugs remain available for legitimate purposes. *See* 21 U.S.C. § 801(1), (2), (7).

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B.

We next consider the specific question of whether DEA may comply with the United States' obligations under the Single Convention by supplementing a decision to place marijuana in Schedule III with regulatory action.

As a threshold matter, we understand that, if marijuana were placed on Schedule III, the gap that DEA would need to fill would be modest. To be sure, the Lawton Memo and the D.C. Circuit expressed concern that placing marijuana into Schedule III would create compliance concerns with respect to certain Single Convention requirements. In its submission to us, however, the State Department observed that, even if marijuana were listed in Schedule III, most of the United States' Single Convention obligations would continue to be met. *See* State Response at 4–7. The State Department's view reflects amendments to the CSA that postdate the Lawton Memo (from 1972) and the D.C. Circuit's consideration of the issue (in 1977) and that specifically authorize certain controls required by the Single Convention to be placed on drugs outside Schedules I and II. Given these amendments, many of the gaps previously identified in Single Convention compliance would no longer exist if marijuana were placed in Schedule III.

In particular, the Lawton Memo and D.C. Circuit both pointed to the manufacturing and import quotas required by Article 21 of the Single Convention as potential gaps, *see* Lawton Memo at 12–13, while the D.C. Circuit also identified the estimates and statistical reports required by Articles 19 and 20 and the import and export authorizations required by Article 31(4), *see NORML II*, 559 F.2d at 751 n.71. In 1978, however, Congress enacted 21 U.S.C. § 827(e), which specifically authorizes the Attorney General, among other things, to prescribe measures necessary to comply with the reporting requirements of Articles 19 and 20 of the Single Convention for drugs in any schedule, not just those in Schedules I and II. *See* Psychotropic Substances Act of 1978, Pub. L. No. 95-633, § 104, 92 Stat. 3768, 3772. In addition, in 1984 Congress amended the CSA provisions that implement the import and export permit requirements to specifically authorize the use of permits for a nonnarcotic Schedule III drug. *See* 21 U.S.C. §§ 952(b)(2), 953(e) (enacted by the Controlled Substances Penalties Amendments Act of 1984, Pub. L. No. 98-473,

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§§ 521–522, 98 Stat. 1837, 2075–76). If marijuana, a nonnarcotic drug, were placed in Schedule III, we believe these statutory provisions would ensure compliance with both the import quota obligation of Article 21 and the import and export authorization requirements of Article 31(4).

These subsequent enactments address most of the concerns the Lawton Memo and D.C. Circuit identified, with the exception of the manufacturing quota requirements of Article 21 of the Convention. But we believe this remaining gap is addressable using the CSA’s regulatory authorities. Several different authorities appear potentially applicable. A regulation imposing a manufacturing quota on a drug would fall easily within the broad language of section 821, as it would be “relat[ed] to the . . . control of the manufacture” of a drug. 21 U.S.C. § 821. DEA likewise could deem a regulation imposing a manufacturing quota as “necessary and appropriate for the efficient execution of” the CSA function of controlling drugs to meet the United States’ international obligations. *Id.* § 871(b); *see id.* § 811(d)(1). By their plain terms, the CSA’s registration authorities would also give DEA the authority to impose a manufacturing quota on a particular drug through regulation: no person can manufacture a drug (including marijuana) without a registration issued by DEA, *see id.* § 822(a), and in that registration DEA can limit the “extent” to which any person is “authorized to . . . manufacture” marijuana under their registration, *id.* § 822(b). Section 823(e) provides yet another potential source of authority for imposing a manufacturing quota on a Schedule III drug, as DEA could conclude under section 823(e) that registrations to manufacture marijuana would be “inconsistent with the public interest” unless a quota consistent with Article 21 of the Single Convention was implemented to maintain “effective controls against diversion.” *Id.* § 823(e); *see also Oregon*, 546 U.S. at 260 (identifying similar language in section 823(a) as providing regulatory authority).⁹

⁹ We note that section 823(a) provides that the Attorney General shall register manufacturers of Schedule I and Schedule II drugs upon determining that “such registration is consistent with the public interest and *with United States obligations under international treaties, conventions, or protocols in effect on May 1, 1971.*” (Emphasis added.) In *Licensing Marijuana Cultivation*, we emphasized section 823(a)’s invocation of international obligations in concluding that DEA could promulgate regulatory controls necessary to meet certain of the United States’ obligations under the Single Convention. *See* 42 Op. O.L.C. __, at *24. Although section 823(e) does not include a similar requirement to

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In concluding that the CSA provides numerous sources of authority that could be used to impose a manufacturing quota, we recognize that section 826 expressly requires manufacturing quotas for drugs in Schedules I and II.¹⁰ But that requirement should not be read as implicitly foreclosing the imposition of such quotas for drugs in Schedules III through V. As the D.C. Circuit has recognized, “a congressional mandate in one section and silence in another often suggests not a prohibition but simply a decision . . . to leave the question to agency discretion.” *Catawba County v. EPA*, 571 F.3d 20, 36 (D.C. Cir. 2009) (per curiam) (quotation marks omitted).

We therefore conclude that both the Single Convention and the CSA permit DEA to place marijuana in Schedule III while imposing additional controls, pursuant to the CSA’s regulatory authorities, to close a modest gap between the requirements of the Single Convention and the requirements that follow from placement on Schedule III.

V.

For the reasons set forth above, we conclude, first, that DEA’s current approach to determining whether a drug has a CAMU is impermissibly narrow, and that satisfying HHS’s two-part inquiry is sufficient to establish that a drug has a CAMU even if the drug has not been approved by

consider international obligations, it does require the Attorney General to consider whether registration is “inconsistent with the public interest,” 21 U.S.C. § 823(e), and complying with the United States’ international obligations is plainly in the public interest. Against this backdrop, we do not read Congress’s silence with respect to international obligations in section 823(e) as precluding DEA from relying on that section to comply with international obligations. See *Catawba County v. EPA*, 571 F.3d 20, 36 (D.C. Cir. 2009) (per curiam).

¹⁰ Although the CSA refers to quotas on the “production” of drugs and the Single Convention to quotas on the “manufacture” of drugs, we understand the scope of these terms to largely overlap. The CSA defines “production” to include the “manufacture, planting, cultivation, growing, or harvesting of a controlled substance,” 21 U.S.C. § 802(22), and, in turn, defines “manufacture” to include the “production, preparation, propagation, compounding, or processing of a drug,” *id.* § 802(15). The Single Convention defines “manufacture” to mean “all processes . . . by which drugs may be obtained and includes refining as well as the transformation of drugs into other drugs,” Single Convention art. 1(1)(n), but excludes “the separation of . . . cannabis and cannabis resin from the plants from which they are obtained,” *id.* art. 1(1)(t).

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FDA and would not satisfy DEA's five-part test. Second, we conclude that HHS's overall CAMU recommendation is not binding on DEA and that the scientific and medical determinations that underlie HHS's CAMU recommendation are binding, but only until the initiation of formal rulemaking proceedings. Once DEA initiates formal rulemaking, HHS's determinations no longer bind DEA, but DEA must continue to accord HHS's scientific and medical determinations significant deference, and the CSA does not allow DEA to undertake a *de novo* assessment of HHS's findings at any point in the process. Finally, we conclude that neither the Single Convention nor the CSA requires marijuana to be placed into Schedule I or II. Both the Single Convention and the CSA allow DEA to satisfy the United States' international obligations by supplementing scheduling decisions with regulatory action, at least in circumstances where there is a modest gap between the Convention's requirements and the specific restrictions that follow from a drug's placement on a particular schedule. As a result, DEA may satisfy the United States' Single Convention obligations by placing marijuana in Schedule III while imposing additional restrictions pursuant to the CSA's regulatory authorities.

CHRISTOPHER C. FONZONE

Assistant Attorney General

Office of Legal Counsel



required by another Federal law or regulation or Federal directive issued in connection with the applicable list. The procedures also must require the investment adviser to follow all Federal directives issued in connection with such lists.

(5)(i) *Customer notice.* The CIP must include procedures for providing customers with adequate notice that the investment adviser is requesting information to verify their identities.

(ii) *Adequate notice.* Notice is adequate if the investment adviser generally describes the identification requirements of this section and provides such notice in a manner reasonably designed to ensure that a prospective customer is able to view the notice, or is otherwise given notice, before opening an account. For example, depending upon the manner in which the account is opened, an investment adviser may post a notice on its website, include the notice in its account applications, or use any other form of oral or written notice.

(iii) *Sample notice.* If appropriate, an investment adviser may use the following sample language to provide notice to its customers:

IMPORTANT INFORMATION ABOUT PROCEDURES FOR OPENING A NEW ACCOUNT

To help the government fight the funding of terrorism and money laundering activities, Federal law requires all financial institutions to obtain, verify, and record information that identifies each natural or legal person who opens an account, which may be an individual or a person other than an individual (such as a corporation, partnership, or trust).

What this means for you: When you open an account, we will ask for the name, address, date of birth or formation, tax identification number, and other information pertaining to the accountholder. This information will help us verify the identity of the accountholder. We may also ask to see identifying documents pertaining to the accountholder, such as a driver's license (if you are an individual) or a business license, articles of incorporation, or trust instrument (if the accountholder is not an individual).

(6) *Reliance on another financial institution.* The CIP may include procedures specifying when the investment adviser will rely on the performance by another financial institution (including an affiliate) of any procedures of the investment adviser's CIP with respect to any customer of the investment adviser that is opening, or has opened, an account or has established an account or similar business relationship with the other financial institution to provide or engage in services, dealings, or other financial transactions, provided that:

(i) Such reliance is reasonable under the circumstances;

(ii) The other financial institution is subject to a rule implementing 31 U.S.C. 5318(h) and regulated by a Federal functional regulator; and

(iii) The other financial institution enters into a contract with the investment adviser requiring it to certify annually to the investment adviser that it has implemented its anti-money laundering/countering the financing of terrorism program, and that it will perform (or its agent will perform) specified requirements of the investment adviser's CIP.

(b) *Exemptions.* The Commission, with the concurrence of the Secretary, may by order or regulation exempt any investment adviser or any type of account from the requirements of this section. The Secretary, with the concurrence of the Commission, may exempt any investment adviser or any type of account from the requirements of this section. In issuing such exemptions, the Commission and the Secretary shall consider whether the exemption is consistent with the purposes of the Bank Secrecy Act, and in the public interest, and may consider other necessary and appropriate factors.

(c) *Effective date.* The effective date is [DATE 60 DAYS AFTER DATE OF PUBLICATION OF THE FINAL RULE IN THE FEDERAL REGISTER]. An investment adviser must develop and implement a CIP that complies with the requirements of this section on or before [DATE 6 MONTHS AFTER EFFECTIVE DATE OF FINAL RULE].

(d) *Other requirements unaffected.* Nothing in this section relieves an investment adviser of its obligation to comply with any other provision of this chapter, including provisions concerning information that must be obtained, verified, or maintained in connection with any account or transaction.

Dated: May 10, 2024.

By the Financial Crimes Enforcement Network.

Andrea M. Gacki,
Director.

Dated: May 13, 2024.

By the Securities and Exchange Commission.

Vanessa A. Countryman,
Secretary.

[FR Doc. 2024-10738 Filed 5-17-24; 11:15 am]

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-1362; A.G. Order No. 5931-2024]

Schedules of Controlled Substances: Rescheduling of Marijuana

AGENCY: Drug Enforcement Administration, Department of Justice.
ACTION: Notice of proposed rulemaking.

SUMMARY: The Department of Justice ("DOJ") proposes to transfer marijuana from schedule I of the Controlled Substances Act ("CSA") to schedule III of the CSA, consistent with the view of the Department of Health and Human Services ("HHS") that marijuana has a currently accepted medical use as well as HHS's views about marijuana's abuse potential and level of physical or psychological dependence. The CSA requires that such actions be made through formal rulemaking on the record after opportunity for a hearing. If the transfer to schedule III is finalized, the regulatory controls applicable to schedule III controlled substances would apply, as appropriate, along with existing marijuana-specific requirements and any additional controls that might be implemented, including those that might be implemented to meet U.S. treaty obligations. If marijuana is transferred into schedule III, the manufacture, distribution, dispensing, and possession of marijuana would remain subject to the applicable criminal prohibitions of the CSA. Any drugs containing a substance within the CSA's definition of "marijuana" would also remain subject to the applicable prohibitions in the Federal Food, Drug, and Cosmetic Act ("FDCA"). DOJ is soliciting comments on this proposal.

DATES: Comments must be submitted electronically or postmarked on or before July 22, 2024. Interested persons may file a request for a hearing or waiver of an opportunity for a hearing or to participate in a hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.47 or 1316.49, as applicable, which must be received or postmarked on or before June 20, 2024.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-1362" on all correspondence, including any attachments.

• *Electronic comments:* DOJ encourages that all comments be submitted through the Federal eRulemaking Portal, which provides the ability to type short comments directly

into the comment field on the web page or to attach a file for lengthier comments. Please go to <https://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on <https://www.regulations.gov>. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

- **Paper comments:** Paper comments that duplicate electronic submissions are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of submitting a comment electronically, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

- **Hearing requests:** All requests for a hearing and waivers, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with DEA. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Drug & Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249; Email: nprm@dea.gov.

SUPPLEMENTARY INFORMATION: To be considered as part of this rulemaking, comments and requests for a hearing must be submitted in response to this proposed rule within the timeframe specified above, regardless of whether the comment, hearing request, or other information was previously submitted to the Drug Enforcement Administration ("DEA") in connection with any prior

matter relating to the scheduling of marijuana.

I. Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. DOJ will make comments available for public inspection online at <https://www.regulations.gov>. Such information includes personal or business identifiers (such as name, address, State or Federal identifiers, etc.) voluntarily submitted by the commenter. Generally, all information voluntarily submitted by the commenter, unless clearly marked as "Confidential Information" in the method described below, will be publicly posted. Comments may be submitted anonymously. The Freedom of Information Act, 5 U.S.C. 552, applies to all comments received.

Commenters submitting comments that include personal identifying information ("PII") or confidential or proprietary business information that the commenter does not want made publicly available should submit two copies of the comment. One copy must be marked "CONTAINS CONFIDENTIAL INFORMATION" and should clearly identify all PII or business information the commenter does not want to be made publicly available, including any supplemental materials. DOJ will review this copy, including the claimed PII and confidential business information, in its consideration of comments. The second copy should be marked "TO BE PUBLICLY POSTED" and must have all claimed confidential PII and business information already redacted. DOJ will post only the version of the comment with redactions on <https://www.regulations.gov> for public inspection.

An electronic copy of this document and supplemental information to this proposed rule are available at <https://www.regulations.gov> for easy reference. DOJ specifically solicits written comments regarding the economic analysis of the impact of these proposed changes. DOJ requests that commenters provide detailed descriptions in their comments of any expected economic impacts, especially to small entities. Commenters should provide empirical data to illustrate the nature and scope of such impact.

II. Request for Hearing, Notice of Appearance at, or Waiver of Participation in Hearing

Pursuant to 21 U.S.C. 811(a), this scheduling action is a formal rulemaking "on the record after opportunity for a hearing." Such

proceedings are conducted pursuant to the Administrative Procedure Act ("APA"), 5 U.S.C. 551-559. See 21 CFR 1308.41 through 1308.45; *id.* part 1316, subpart D. Interested persons, as defined in 21 CFR 1300.01(b), may file requests for a hearing in conformity with the requirements of 21 CFR 1308.44(a) and 1316.47(a), and such requests must:

- (1) state with particularity the interest of the person in the proceeding;
- (2) state with particularity the objections or issues concerning which the person desires to be heard; and
- (3) state briefly the position of the person regarding the objections or issues.

All requests for a hearing and waivers of an opportunity for a hearing or participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above.

The decision whether an in-person hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator of DEA. Upon the Administrator's determination to grant an in-person hearing, DEA will publish a notice of hearing on the proposed rulemaking in the **Federal Register**. See 21 CFR 1308.44(b), 1316.53.

If the Administrator determines to grant an in-person hearing to address such matters of fact and law in this rulemaking, the Administrator will then designate an Administrative Law Judge ("ALJ") to preside over the hearing. The ALJ's functions shall commence upon designation, as provided in 21 CFR 1316.52. The ALJ will have all powers necessary to conduct a fair hearing, to take all necessary action to avoid delay, and to maintain order. *Id.* The ALJ's authorities include the power to hold conferences to simplify or determine the issues in the hearing or to consider other matters that may aid in the expeditious disposition of the hearing; require parties to state their position in writing; sign and issue subpoenas to compel the production of documents and materials to the extent necessary to conduct the hearing; examine witnesses and direct witnesses to testify; receive, rule on, exclude, or limit evidence; rule on procedural items; and take any action permitted by the presiding officer under DEA's hearing procedures and the APA. *Id.*

Comments on or objections to the proposed rule submitted under 21 CFR 1308.43(g) will be offered as evidence at the hearing, but the presiding officer shall admit only evidence that is competent, relevant, material, and not unduly repetitive. 21 CFR 1316.59(a).

Any interested person may file a waiver of opportunity for a hearing or to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(c), together with a written statement of position on the matters of fact and law involved in any hearing. 21 CFR 1316.49. Such statement, if admissible, will be included in the record and considered as described in 21 CFR 1308.44(c).

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to “receiv[e] factual evidence and expert opinion regarding” whether marijuana should be transferred to schedule III of the list of controlled substances. 21 CFR 1308.42. Concurrent with this rulemaking, DEA will consider the marijuana-specific controls that would be necessary to comply with relevant treaty obligations in the event that, after the hearing, a final order reschedules marijuana, and, to the extent such controls are needed if marijuana is rescheduled, will seek to finalize any such regulations as soon as possible.

All requests for hearing and waivers of an opportunity for a hearing or participation must be sent to DEA using the address information above, on or before the date specified above.

III. Legal Authority

Under the CSA, 21 U.S.C. 801 *et seq.*, the Attorney General shall, before initiating proceedings to control, decontrol, or transfer between schedules a drug or other substance, request from the Secretary of HHS a scientific and medical evaluation, and the Secretary’s recommendations, as to whether such drug or other substance should be so controlled or removed as a controlled substance. 21 U.S.C. 811(b). The recommendations of the Secretary shall include recommendations with respect to the appropriate schedule, if any, under which such drug or other substance should be listed. *Id.*

HHS recommended in August 2023 that marijuana be rescheduled to schedule III. *See* Letter for Anne Milgram, Administrator, DEA, from Rachel L. Levine, M.D., Assistant Secretary for Health, HHS (Aug. 29, 2023) (“August 2023 Letter”). The Attorney General then sought the legal advice of the Office of Legal Counsel (“OLC”) at DOJ on questions relevant to this rulemaking proceeding. Among other conclusions, OLC concluded that “HHS’s scientific and medical determinations must be binding until issuance of a notice of proposed rulemaking [(‘NPRM’)].” *Questions Related to the Potential Rescheduling of Marijuana*, 45 Op. O.L.C. ___, at *25

(Apr. 11, 2024) (“OLC Op.”).¹ After the issuance of a notice of rulemaking proceedings, HHS’s scientific and medical determinations are accorded “significant deference” through the rest of the rulemaking process.² OLC Op. at *26.

Under the CSA, when recommending or determining that a drug should be controlled (and if so, under which schedule), the Secretary and the Attorney General must consider eight factors set forth in 21 U.S.C. 811(c). The eight factors are:

1. The drug’s actual or relative potential for abuse;
 2. Scientific evidence of its pharmacological effect, if known;
 3. The state of current scientific knowledge regarding the drug or other substance;
 4. Its history and current pattern of abuse;
 5. The scope, duration, and significance of abuse;
 6. What, if any, risk there is to the public health;
 7. Its psychic or physiological dependence liability; and
 8. Whether the substance is an immediate precursor of a substance already controlled.
- 21 U.S.C. 811(c); *see also id.* 811(b) (specifying how HHS should consider each of the eight factors).

The United States is a party to the 1961 United Nations Single Convention on Narcotic Drugs, March 30, 1961, 18 U.S.T. 1407, 520 U.N.T.S. 151 (“Single Convention”), as amended by the 1972 Protocol, March 25, 1972, 26 U.S.T. 1439, 976 U.N.T.S. 3. Under 21 U.S.C. 811(d)(1), if control of a substance is required “by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970,” the Attorney General must issue an order controlling such drug “under the schedule he deems most appropriate to carry out such

obligations, without regard to the findings” required by 21 U.S.C. 811(a) or 812(b), “and without regard to the procedures” prescribed by 21 U.S.C. 811(a) and (b). Marijuana is a drug covered by the Single Convention. *See* Single Convention art. 1(1)(b); OLC Op. at *26 & n.7.

OLC and the United States Court of Appeals for the D.C. Circuit have explained that section 811(d)(1) does not supersede the scheduling procedures set forth in sections 811(a) through (b) and 812(b), including the requirement to consider the eight factors set forth in section 811(c). Instead, section 811(d)(1) allows the Attorney General to “identify which schedules would satisfy the United States’ international obligations with respect to a particular drug, and then—if more than one schedule would do so—select which schedule to use through the section 811(a) through (b) and 812(b) procedures.” OLC Op. at *29 n.8; *accord Nat’l Org. for Reform of Marijuana Laws (NORML II) v. DEA*, 559 F.2d 735, 747 (D.C. Cir. 1977). HHS performed the eight-factor analysis. *See* Memorandum for DEA, from HHS, *Re: Basis for the Recommendation to Reschedule Marijuana to Schedule III of the Controlled Substances Act* (“HHS Basis for Rec.”). As noted above, HHS’s scientific and medical determinations are binding on DOJ until an NPRM is published, and, in addition, DOJ must accord “significant deference” to HHS’s scientific and medical determinations throughout the rulemaking process. OLC Op. at *25–26.

Once the determination is made that a particular drug or substance must be controlled under the CSA, the Attorney General must determine the level of control over the drug or substance under the CSA. *See* 21 U.S.C. 811(a), (b). The CSA divides controlled substances into five levels of control, or “schedules,” based on (1) a drug’s potential for abuse, (2) whether the drug has a currently accepted medical use in treatment in the United States (“CAMU”), and (3) whether there is a lack of accepted safety for use of the drug under medical supervision or the level of psychological or physical dependence that could result from abuse of the drug. *See id.* 812(b). Schedule I drugs have a high potential for abuse, no CAMU, and a lack of accepted safety for use under medical supervision. *Id.* 812(b)(1). Schedule II drugs also have a high potential for abuse but have a CAMU (or a CAMU with “severe restrictions”), and abuse of the drug may lead to severe psychological or physical dependence. *Id.* 812(b)(2). Schedule III drugs, meanwhile, have a lower potential for

¹ OLC’s opinion is available in its entirety under “Supporting and Related Material” of the public docket for this proposed rule at <https://www.regulations.gov> under docket number DEA–1362.

² The CSA’s reliance on formal rulemaking for scheduling decisions indicates that HHS’s determinations do not bind DOJ for the entirety of the rulemaking process, because outside participants may submit additional scientific and medical evidence during the rulemaking that DOJ would need to consider. OLC Op. at *25. However, DOJ “may not simply cast aside HHS’s scientific and medical recommendations once it initiates rulemaking proceedings by issuing an NPRM,” since “[t]he categorical use of the word ‘binding’ in section 811(b) suggests that Congress intended HHS’s scientific and medical views to at least be a very significant input in the scheduling process,” and the legislative history of the CSA bolsters that conclusion. *Id.* at 25–26 (citing H.R. Rep. No. 91–1444, at 22–23 (1970)).

abuse when compared to drugs in schedules I and II, have a CAMU, and their abuse may lead to moderate or low physical dependence or high psychological dependence.³ 21 U.S.C. 812(b)(3). The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by 21 U.S.C. 812(b) for the schedule in which such drug is to be placed. The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General on his own motion, at the request of the Secretary, or on the petition of any interested party. *Id.*

IV. Background

When Congress enacted the CSA in 1970, it placed marijuana in schedule I. Comprehensive Drug Abuse Prevention and Control Act of 1970, Public Law 91–513, tit. II, sec. 202(c), 84 Stat. 1236, 1249 (1970); 21 U.S.C. 812(c).⁴ The Attorney General is authorized to amend this initial placement. 21 U.S.C. 812(c); *see also id.* 811, 812(b). Other schedule I substances include heroin, lysergic acid diethylamide (commonly known as LSD), and 3,4-methylene dioxymethamphetamine (ecstasy). *See* 21 CFR 1308.11. Drugs controlled under schedule II include cocaine, methamphetamine, methadone, oxycodone, and fentanyl. *Id.* § 1308.12. Drugs controlled under schedule III include products containing less than 90 milligrams of codeine per dosage unit, ketamine, and anabolic steroids. *Id.* § 1308.13. Petitioners have requested that marijuana be rescheduled several times over the years. *See, e.g., Schedule of Controlled Substances: Petition To*

Remove Marihuana From Control or in the Alternative To Control Marihuana in Schedule V of the Controlled Substances Act, 37 FR 18097 (Sept. 7, 1972); *Notice of Denial of Petition*, 66 FR 20038 (Apr. 18, 2001); *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 76 FR 40552 (July 8, 2011).

DEA and HHS last examined the issue of whether to reschedule marijuana eight years ago, in 2016, when DEA denied two petitions to reschedule marijuana.⁵ At the time, HHS concurred that marijuana should remain a schedule I drug because it met the three criteria for placement in schedule I. 81 FR 53706–07. In accordance with the requirements for placement in schedule I, HHS found that: (1) marijuana had a high potential for abuse; (2) it did not have a CAMU; and (3) there was a lack of accepted safety for use of marijuana under medical supervision. *Id.* As discussed in detail below, in 2023, HHS conducted a scientific and medical evaluation of marijuana based on a comprehensive review of available data at that time and recommended that marijuana be transferred to schedule III.

Since 1996, 38 States, the District of Columbia, and 4 Federal Territories have legalized the use of medical marijuana. HHS Basis for Rec. at 30; OLC Op at *9. These laws typically allow the cultivation, sale, and use of marijuana by patients (or their caregivers) whose health care practitioners have recommended that they use marijuana to treat certain health conditions. *See, e.g.,* Ohio Rev. Code secs. 3796.01(A)(6)(a)–(v), 3796.01(A); N.Y. Cannabis Law secs. 3(18), 30, 31; N.M. Stat. secs. 26–2B–3(F)(1)–(23), 26–2B–3(N), 26–2B–4(A). Further, beginning in Fiscal Year 2015, Congress has adopted an appropriations rider every year that prohibits DOJ from using funds to prevent certain States, Territories, and the District of Columbia from implementing their own laws with respect to medical marijuana. *E.g.,* Consolidated Appropriations Act, 2024, Public Law 118–42, sec. 531, 138 Stat. 25; Consolidated Appropriations Act, 2023, Public Law 117–328, sec. 531, 136 Stat. 4459, 4561 (2022); *see also* Cong. Research Serv., R44782, *The Evolution of Marijuana as a Controlled Substance and the Federal-State Policy Gap* 26 & n.159 (updated Apr. 7, 2022) (collecting additional appropriations riders).

Marijuana is generally defined by statute to mean “the plant *Cannabis*

sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.” 21 U.S.C. 802(16)(A). In 2018, Congress amended the CSA to remove “(i) hemp, as defined in section [1639o] of title 7 of the U.S. Code]” from the definition of marijuana.⁶ Agricultural Improvement Act of 2018, Public Law 115–334, sec. 12619, 132 Stat. 4490, 5018. Section 1639o(1) of title 7 in turn defines hemp as “the plant *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9-tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.” Delta-9-tetrahydrocannabinol (“Δ9-THC”) is the major psychoactive intoxicating cannabinoid in marijuana. *See* HHS Basis for Rec. at 10. This exclusion of hemp from the definition of marijuana had the effect of removing many products containing predominantly cannabidiol (“CBD”) derived from hemp and containing no more than 0.3 percent Δ9-THC on a dry weight basis from control as marijuana.

On October 6, 2022, President Biden requested that the Attorney General and the Secretary of HHS “initiate the administrative process to review expeditiously how marijuana is scheduled under federal law.”⁷ HHS thereafter undertook a scientific and medical evaluation of marijuana as defined under the CSA in accordance with the President’s request.

In a letter dated August 29, 2023, Admiral Rachel L. Levine, M.D., HHS’s Assistant Secretary for Health, recommended to the Administrator of DEA that marijuana be controlled in schedule III of the CSA. August 2023 Letter. HHS found that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II; that marijuana has a CAMU; and that the abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence. HHS

³ Schedule IV includes drugs that have a low potential for abuse relative to those in schedule III, that have a CAMU, and for which abuse may lead to limited physical or psychological dependence relative to those in schedule III. 21 U.S.C. 812(b)(4). Schedule V includes drugs that have a low potential for abuse relative to those in schedule IV, that have a CAMU, and for which abuse may lead to limited physical or psychological dependence relative to those in schedule IV. *Id.* 812(b)(5).

⁴ The CSA refers to the drug as “marijuana” and “marihuana” interchangeably. *See, e.g.,* 21 U.S.C. 802(16)(A), 812(c). As used in this NPRM, “marijuana” means the term defined at 21 U.S.C. 802(16).

⁵ *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 81 FR 53688 (Aug. 12, 2016); *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 81 FR 53767 (Aug. 12, 2016).

⁶ Marijuana under the CSA also does not include “the mature stalks of [the cannabis] plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of [the cannabis] plant which is incapable of germination.” 21 U.S.C. 802(16)(B)(ii).

⁷ The White House, *Statement from President Biden on Marijuana Reform* (Oct. 6, 2022), <https://www.whitehouse.gov/briefing-room/statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform/>.

Basis for Rec. at 62–65. These findings correspond to the criteria for placement of a substance in schedule III. *See* 21 U.S.C. 812(b)(3). DEA has not yet made a determination as to its views of the appropriate schedule for marijuana.

V. Proposal To Reschedule Marijuana

The CSA vests the Attorney General with the authority to schedule, reschedule, or decontrol drugs. 21 U.S.C. 811(a). The Attorney General has delegated that authority to the DEA Administrator, *see* 28 CFR 0.100, but also retains the authority to schedule drugs under the CSA in the first instance, *see* 28 U.S.C. 509, 510. The HHS Assistant Secretary for Health has provided a recommendation for transferring marijuana to schedule III. In light of that recommendation, the Attorney General is exercising the Attorney General's authority under 21 U.S.C. 811(a) to initiate a rulemaking that proposes the placement of marijuana in schedule III.

DEA believes that additional information arising from this rulemaking will further inform the findings regarding the appropriate schedule for marijuana. DEA has maintained an active review of the scientific literature addressing marijuana with a focus on how it relates to the scientific and medical evaluation and informs any updates to the eight-factor analysis. In addition to HHS's scientific and medical determinations, which are binding until the issuance of this NPRM and which must be accorded significant deference throughout the rulemaking, DEA believes that factual evidence (including scientific data) and expert opinions, including additional data regarding different forms, formulations, and delivery methods for marijuana, as well as evidence regarding the effects of marijuana at various dosages or concentrations, may be relevant.

The HHS Basis for Recommendation, DEA's analyses explaining its decisions to deny the petitions to reschedule marijuana in 2016, and the 2024 OLC opinion (cited throughout) are available in their entirety under "Supporting and Related Material" of the public docket for this proposed rule at <https://www.regulations.gov> under docket number DEA–1362.

VI. Eight-Factor Analysis

DOJ has reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS and has conducted a separate review of the eight factors identified in 21 U.S.C. 811(c). At this point in the proceedings, DOJ must treat HHS's scientific and

medical determinations as binding. *See* OLC Op. at *4, *25. HHS's scientific and medical determinations are included below, as well as certain information from DEA.

1. Marijuana's Actual or Relative Potential for Abuse

The first factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the actual or relative potential for abuse of marijuana. The term "abuse" is not defined in the CSA. However, consistent with the legislative history of the CSA, DEA and HHS have typically weighed the following factors in determining whether a particular drug or substance has a potential for abuse:⁸

A. Whether there is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

As part of its analysis, HHS concluded that evidence shows that, although some individuals are taking marijuana in amounts sufficient to create a hazard to their health and to the safety of other individuals and the community, the vast majority of individuals who use marijuana are doing so in a manner that does not lead to dangerous outcomes to themselves or others. HHS Basis for Rec. at 6–7. The data supportive of this conclusion are discussed in detail in HHS's analysis of Factors 4, 5, and 6. *See* HHS Basis for Rec. at 28–57.

In particular, HHS emphasized that an evaluation of various epidemiological databases of adverse outcomes from 2015 to 2021 involving marijuana or comparator drugs that are used nonmedically showed that the utilization-adjusted rate of adverse outcomes involving marijuana was consistently lower than the utilization-adjusted rates of adverse outcomes involving heroin, cocaine, and, for certain outcomes, other comparators, including alcohol. Also, alcohol or heroin typically ranked first or in immediately subsequent positions among the comparators in terms of incidence of adverse outcomes, with marijuana in a lower place in that ranking. This pattern also was observed for serious medical outcomes, including death, observed in Poison Center data, where marijuana was in the lowest ranking group. This suggests consistency across databases, across drugs, and over time. HHS thus

concluded that although abuse of marijuana produces clear evidence of harmful consequences, these appear to be relatively less common and less severe than the consequences of some other comparator substances. HHS Basis for Rec. at 7–8.

Importantly, these comparisons of the prevalence of adverse outcomes were from descriptive analyses only, following the established practice in previous eight-factor analyses. Thus, differences in outcome frequency and severity, and the ranked order across comparators, may be attributable in part to underlying differences in the populations being compared (e.g., age or pre-existing medical conditions), among other things. Despite these limitations, qualitative synthesis of descriptive analyses is the established practice in previous eight-factor analyses, and HHS determined that it is the most appropriate approach here. HHS Basis for Rec. at 7–8.

HHS also concluded that the public-health risks posed by marijuana are lower compared to those posed by other drugs of abuse (e.g., heroin, oxycodone, cocaine), based on HHS's evaluation of various epidemiological databases for emergency department ("ED") visits, hospitalizations, unintentional exposures, and most importantly, overdose deaths. The rank order of the comparators in terms of greatest adverse consequences typically ranked heroin, benzodiazepines, and cocaine first or in immediately subsequent positions, with marijuana in a lower place in the ranking, especially when HHS adjusted for utilization. For overdose deaths, marijuana is always in the lowest ranking among comparator drugs. These evaluations demonstrate that there is consistency across databases, across substances, and over time. HHS thus concluded that although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs. HHS Basis for Rec. at 7–8.

DEA notes that data provided by HHS in its recommendation included a 2023 national survey that tracks drug use trends among 8th-, 10th-, and 12th-grade students, and showed that by 12th grade, 20.2 percent of students reported using marijuana in the past month.⁹ DEA also notes that the same study showed that the prevalence of ingesting marijuana by vaping is evidenced by

⁸ *See, e.g.*, 81 FR 53740; *see also* HHS Basis for Rec. at 6 (citing Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444 (1970), reprinted in 1970 U.S.C.A.N. 4566, 4603).

⁹ *See* HHS Basis for Rec. at 35 (discussing Richard A. Miech et al., Univ. of Mich. Inst. for Soc. Rsch., *Monitoring the Future: National Survey Results on Drug Use, 1975–2022: Secondary School Students* 71 (2023), <https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022.pdf>).

students reporting vaping in the 30 days prior at the following rates: 4.2 percent for 8th graders, 10.3 percent for 10th graders, and 14.8 percent for 12th graders.¹⁰ In 2022, the Substance Abuse and Mental Health Services Administration's ("SAMHSA") Drug Abuse Warning Network ("DAWN") reported that 11.9 percent of drug-related ED visits nationwide involved cannabis.¹¹ The rate of cannabis-related ED visits was highest in these demographic groups: 18 to 25 years old, male, Black or African American, and Not Hispanic or Latino.¹²

In addition to the data considered by the HHS Basis for Recommendation, the data considered by HHS and DEA in their 2015 eight-factor analysis, and the additional data discussed above, DEA anticipates that additional data on seizures of marijuana by law enforcement, cannabis-related ED visits, as well as updated epidemiological survey data since 2022, may be appropriate for consideration.

B. Whether there is significant diversion of the drug or drugs containing such a substance from legitimate drug channels.

HHS found that there is a lack of evidence of significant diversion of marijuana from legitimate drug channels. HHS Basis for Rec. at 8. It noted that marijuana is used by researchers for clinical research under investigational new drug ("IND") applications, and that there are multiple DEA registrants that are approved to produce marijuana and derived formulations for use in DEA-authorized nonclinical and clinical research. HHS observed that these authorizations represent the only federally sanctioned drug channels in the United States, and there is a lack of data indicating diversion occurring from these entities or activities. However, there are significant additional sources of marijuana in the United States, including from illicit cultivation and production, illicit importation from other countries, and from State programs that permit dispensing of marijuana for medical use and, in some States, recreational adult use. HHS Basis for Rec. at 8.

Given this unique landscape, DEA believes that the lack of data indicating diversion of marijuana from federally sanctioned drug channels to the illicit market is not indicative of a lack of

potential for abuse of the drug. DEA anticipates that additional data on diversion from State programs and DEA-registered manufacturers may aid in a determination of whether diversion is taking place.

C. Whether individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of their professional practice.

As HHS notes, the Food and Drug Administration ("FDA") has not approved a New Drug Application ("NDA") for a drug product containing botanical marijuana for any therapeutic indication. Thus, the only way an individual can use marijuana on the basis of medical advice through legitimate channels under Federal law is by participating in research under an IND. However, 38 States and the District of Columbia have enacted laws allowing individuals to use marijuana under certain circumstances for medical purposes. Outside of the Federal- and State-sanctioned medical use of marijuana, individuals are using marijuana on their own initiative for medical, as well as nonmedical, purposes. Epidemiological data related to nonmedical use of marijuana is detailed in HHS's analysis of Factor 4. HHS Basis for Rec. at 8.

DEA notes that data is not available to determine the number of individuals using marijuana under State law. According to 2022 National Survey on Drug Use and Health ("NSDUH") data on people who are 12 and older in the United States, 61.9 million people reported using marijuana in the past year, and marijuana was the illicit drug used with the greatest frequency.¹³ Specifically, 42.3 million people reported use in the past month, including 14.7 million people who vaped marijuana in that same period, representing 5.2 percent of the study's target population.¹⁴ Furthermore, as reported by NSDUH in 2022, 3.7 million people initiated marijuana use in the past year, with more than half (53 percent or 2.0 million people) initiating marijuana use before the age of 21.¹⁵ DEA also notes that HHS concluded that, outside of the Federal- and State-sanctioned medical use of marijuana, individuals are using marijuana on their

own initiative for medical as well as nonmedical purposes. HHS Basis for Rec. at 8. In 2016, DEA reached a similar conclusion.¹⁶ In addition to the data considered in the HHS Basis for Recommendation, and by HHS and DEA in their earlier eight-factor analyses, DEA anticipates that updated epidemiological survey data since 2022 may be appropriate for consideration.

D. Whether the drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that it will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that they have a substantial capability of creating hazards to the health of the user or to the safety of the community.

Marijuana has been a schedule I substance since the CSA was enacted in 1970. *See* Public Law 91-513, tit. II, sec. 202(c), 84 Stat. 1236, 1249 (1970); 21 U.S.C. 812(c); *see also* 21 CFR 1308.11(d)(23). The primary compound in marijuana that is responsible for its abuse potential is Δ 9-THC (also known as dronabinol, when specifically referring to the (-)-*trans*- Δ 9-THC stereoisomer), which has agonist activity at cannabinoid CB₁ receptors. HHS found that there are extensive nonclinical and clinical studies establishing that marijuana, due to the CB₁ agonist activity of its main cannabinoid constituent Δ 9-THC, produces rewarding effects that would be consistent with observed long-term patterns of nonmedical use and abuse, both before and in the years since enactment of the CSA. HHS Basis for Rec. at 9. For further discussion of these effects, *see* HHS Basis for Rec. at 9–18 (Factor 2), 28–37 (Factor 4).

Additionally, FDA has approved two drug products containing dronabinol: Marinol (in 1985; schedule III) and Syndros (in 2016; schedule II). HHS Basis for Rec. at 9. Marinol was approved by FDA in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who did not respond to conventional anti-emetic treatments. FDA approved Marinol in 1992 for the treatment of anorexia associated with weight loss in patients with acquired

¹⁰ Miech et al., *supra* note 9, at 75.

¹¹ Drug Abuse Warning Network, Substance Abuse & Mental Health Servs. Admin., *Findings from Drug-Related Emergency Department Visits, 2022*, at 1 (2023), <https://store.samhsa.gov/sites/default/files/pep23-07-03-001.pdf>.

¹² *Id.* at 27.

¹³ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health* 14 (Nov. 2023), <https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-nnr.pdf>.

¹⁴ *Id.* at 13.

¹⁵ *Id.* at 27.

¹⁶ 81 FR 53691 ("Based on the large number of individuals reporting current use of marijuana and the lack of an FDA-approved drug product in the United States, one can assume that it is likely that the majority of individuals using marijuana do so on their own initiative rather than on the basis of medical advice from a licensed practitioner.").

immunodeficiency syndrome (“AIDS”). After the first FDA approval, Marinol was transferred from schedule I to schedule II and was later rescheduled to schedule III. Syndros, a drug product also containing dronabinol but formulated in an oral solution, was approved by FDA in 2016 for the treatment of anorexia associated with weight loss in patients with AIDS, as well as nausea and vomiting associated with cancer chemotherapy in patients who failed to respond adequately to conventional anti-emetic treatments. In 2017, DEA rescheduled “FDA-approved products containing dronabinol in an oral solution” from schedule I into schedule II. HHS Basis for Rec. at 4.

When Marinol and Syndros were being developed, they underwent a systematic evaluation of their abuse potential based on animal and human behavioral studies, which showed that dronabinol has abuse potential. The abuse-related studies confirmed the abuse potential of Δ^9 -THC. HHS has concluded that these findings suggest that marijuana will continue to be used nonmedically, diverted from legitimate channels, and trafficked in illicit channels as a potential source for continued nonmedical use in the United States. HHS Basis for Rec. at 9; *see also* HHS Basis for Rec. at 37–45 (Factor 5).

HHS Conclusion With Respect to Factor 1

HHS determined that epidemiological data indicate that marijuana has the potential for creating hazards to the health of the user and to the safety of the community. However, as a relative finding on abuse liability, when comparing marijuana to heroin, oxycodone, hydrocodone, fentanyl, cocaine, ketamine, benzodiazepines, zolpidem, tramadol, and alcohol in various epidemiological databases that allow for some or all of these comparisons, marijuana is not typically among the substances producing the most frequent incidence of adverse outcomes or severity of substance use disorder. HHS Basis for Rec. at 9; *see also* HHS Basis for Rec. at 28–57 (Factors 4, 5, and 6). But as noted above, there are limitations in comparing descriptive data on adverse outcomes across drugs, although descriptive analyses of epidemiologic data are an established practice in previous eight-factor analyses. HHS Basis for Rec. at 9.

In 2016, DEA found that “[m]arijuana has a high potential for abuse. Preclinical and clinical data show that it has reinforcing effects characteristic of drugs of abuse. . . . Data on marijuana seizures show widespread availability and trafficking.” 81 FR 53739. DEA

believes that additional data in this area may be appropriate for consideration in assessing marijuana’s actual or relative potential for abuse.

2. Scientific Evidence of Marijuana’s Pharmacological Effects, If Known

The second factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the scientific evidence of marijuana’s pharmacological effects, if known. In making its recommendation, HHS considered the scientific evidence of the pharmacological effects of marijuana based on the effects of Δ^9 -THC. HHS conducted a scientific evaluation of the neurochemistry, receptor pharmacology, animal abuse-related behavioral effects, and human behavioral and physiological effects of marijuana. HHS Basis for Rec. at 9.

A. Neurochemistry and Receptor Pharmacology of Marijuana

Cannabis is the genus of a plant that contains numerous natural constituents, including cannabinoids. *See* HHS Basis for Rec. at 18–21 (discussing Factor 3). Because cultivated chemovars may vary in their composition and concentration of various chemical constituents, including with respect to whether they contain significant amounts of Δ^9 -THC or other cannabinoids, marijuana products from different strains will have differing biological and pharmacological profiles. HHS Basis for Rec. at 10.

Marijuana contains at least 560 identified natural constituents, including 125 compounds classified as cannabinoids. Most major cannabinoid compounds occurring naturally in cannabis have been identified chemically, but new and minor compounds are continuously being characterized. HHS Basis for Rec. at 10.

The two most abundant cannabinoids present in marijuana are Δ^9 -THC and CBD. Δ^9 -THC is the major psychoactive intoxicating cannabinoid in marijuana and is the component of marijuana that is primarily responsible for its abuse potential. In contrast, CBD has negligible abuse potential, as assessed by FDA during the NDA review for Epidiolex, an FDA-approved drug product containing plant derived, highly purified CBD. HHS Basis for Rec. at 10.

There are two cannabinoid receptors: CB₁ and CB₂. CB₁ and CB₂ receptors belong to the family of G-protein-coupled receptors and present a typical seven transmembrane-spanning domain structure. Cannabinoid receptors primarily link to an inhibitory G protein (G_{i/o}), such that adenylate cyclase activity is inhibited when a cannabinoid ligand binds to the receptor. This, in

turn, prevents the conversion of adenosine triphosphate to the second messenger, cyclic AMP (“cAMP”), which decreases cAMP levels. As HHS’s analysis described, G proteins also contain beta/gamma G protein units that are also liberated following ligand binding, which then bind to and alter ion channel function, including inhibition of voltage-gated ion channels and activation of potassium channels. Ligand binding can also activate some subforms of phospholipase C as well as beta-arrestin protein. All of these second messenger routes amplify the neural signal following cannabinoid binding at the CB₁ and CB₂ receptors. HHS Basis for Rec. at 10.

CB₁ receptors are found primarily in the central nervous system (“CNS”), but are also present in peripheral tissues, such as the liver, heart, and lungs. In the brain, CB₁ receptors are expressed with highest density in the cortical regions, hippocampus, basal ganglia, and cerebellum and with lowest density in brainstem and hypothalamic areas. The localization of these receptors may explain cannabinoid effects on movement coordination, memory, and cognition. Additionally, CB₁ receptors are found in glial cells as well as in the immune system. However, the concentration of CB₁ receptors is considerably lower in peripheral tissues than in the CNS. CB₂ receptors are found primarily in the immune system, including in numerous leukocyte cell types, as well as in activated CNS microglia. Additionally, there is some evidence that CB₂ receptors are localized in the brain, primarily in the cerebellum and hippocampus. The distribution of CB₂ receptors throughout the body is less extensive than the distribution of CB₁ receptors. HHS Basis for Rec. at 10–11.

There are two endogenous cannabinoid receptor agonists: anandamide and arachidonyl glycerol (“2-AG”). At CB₁ receptors, anandamide is a partial agonist with low intrinsic efficacy while 2-AG is a full agonist with high intrinsic efficacy. These endogenous cannabinoid ligands are present in central as well as peripheral tissues. A combination of uptake and hydrolysis terminates the action of anandamide and 2-AG. The endogenous cannabinoid system is a locally active signaling system activated on demand in response to changes to the local conditions to help restore homeostasis. The endogenous cannabinoid system, including the endogenous cannabinoids and the cannabinoid receptors, demonstrates substantial plasticity in response to several physiological and pathological

stimuli. This plasticity is particularly evident in the CNS. HHS Basis for Rec. at 11.

Δ^9 -THC and CBD have varying affinity and effects at the cannabinoid receptors. HHS determined that Δ^9 -THC is a partial agonist at both CB₁ (K_i = 18–218 nM) and CB₂ receptors (K_i = 36–309 nM). However, CB₁ receptors are the main pharmacological site of action for Δ^9 -THC, making CB₁ receptors the site that is responsible for the abuse potential of marijuana. The other CNS site where Δ^9 -THC may have activity is the 5HT₃ receptor, where it functions as an antagonist. In contrast, CBD has low affinity for both CB₁ and CB₂ receptors and may act as a negative allosteric modulator or weak antagonist at these sites. CBD has additional CNS effects as a serotonin 5HT_{1A} agonist and a serotonin 5HT_{2A} weak partial agonist, as well as a serotonin 5HT_{3A} antagonist. HHS Basis for Rec. at 11.

In the past 30 years, the potency of marijuana with regard to Δ^9 -THC has increased dramatically. HHS described one study finding that the concentration of Δ^9 -THC in marijuana samples in the United States increased from 3 percent in 1991 to 17.1 percent in 2017. These increases are likely due to an increase in the number of high potency samples (*i.e.*, sinsemilla) in the overall samples tested. Based on an evaluation of marijuana seized by DEA, the majority of samples contained high concentrations of Δ^9 -THC and low concentrations of CBD. HHS Basis for Rec. at 11–12.

B. Animal Abuse-Related Behavioral Effects

Self-Administration

Self-administration is a method that assesses the ability of a drug to produce rewarding effects. The presence of rewarding effects increases the likelihood that individuals will try to obtain additional quantities of a drug. Animal self-administration of a drug is often useful in suggesting whether humans will experience a particular substance as having rewarding effects, which is indicative of abuse potential. For example, the tendency of rhesus monkeys to self-administer a drug is correlated with humans' propensity to abuse it. HHS Basis for Rec. at 12.

Since self-administration is a methodology in which the test drug is typically administered intravenously to rats, it is not possible to evaluate botanical marijuana through self-administration. However, given that Δ^9 -THC is the primary substance that confers abuse potential to marijuana, its ability to induce self-administration can

serve as an indicator of the abuse potential of marijuana. HHS Basis for Rec. at 12.

HHS concluded, after weighing the relevant scientific evidence, that Δ^9 -THC produces rewarding effects that lead an animal to repeatedly seek out the substance. HHS Basis for Rec. at 12. Specifically, some studies have demonstrated successful animal self-administration of Δ^9 -THC following intravenous administration, administration of inhaled vapor, oral administration, and intracerebroventricular administration. Other recent animal studies have not been able to produce Δ^9 -THC self-administration following intravenous administration and oral administration, but HHS concluded that these results were due to the specific methodology of those respective studies, rather than valid evidence of the rewarding effects of Δ^9 -THC, and thus do not negate HHS's reliance on studies in which Δ^9 -THC was actively self-administered by animals. HHS Basis for Rec. at 12–13.

Furthermore, a comprehensive deconstruction of which animal methodology is optimal for producing preclinical self-administration of Δ^9 -THC is not necessary for an evaluation of the abuse potential of marijuana in humans because it is already clear that humans utilize marijuana for its rewarding properties. HHS Basis for Rec. at 13. Animal self-administration is used primarily to predict whether a novel substance is likely to be used by humans for its rewarding properties as an indication of its abuse potential. However, epidemiological data already amply demonstrates that humans self-administer substances that contain Δ^9 -THC, including botanical marijuana, for their ability to produce positive subjective responses, including euphoria. HHS Basis for Rec. at 13; *see also* sections VI.4–6 of this preamble (discussing Factors 4–6).

Conditioned Place Preference

A conditioned place preference (“CPP”) study is another method for determining whether drugs have rewarding properties; a CPP study relies on an animal's decision to spend time in a location associated with receiving a drug. The studies in which Δ^9 -THC successfully produced CPP occurred under very specific experimental conditions, similar to the Δ^9 -THC self-administration studies in animals. Experimental manipulations in CPP studies with Δ^9 -THC have included varying the animal species, sex, dose, or route of administration; introducing flavors to obscure unpleasant taste; and varying the drug history of the animals

tested. However, as with animal self-administration, the purpose of CPP studies is typically to determine if a new drug produces rewarding sensations, which would suggest that a drug has abuse potential in humans. Since it is clear that humans self-administer substances that contain Δ^9 -THC, including botanical marijuana, HHS determined that it was not necessary to determine which CPP methods are optimal for demonstrating that Δ^9 -THC has rewarding properties in animals. HHS Basis for Rec. at 13.

Drug Discrimination Studies

Drug discrimination is a method in which animals indicate whether a test drug produces sensations similar to those produced by a training drug with a known pharmacological mechanism of action. Drug discrimination is considered to be an abuse-related study only when the training drug is a known drug of abuse that is scheduled under the CSA and the test drug may have abusable effects similar to the training drug based on having a similar mechanism of action to the training drug. Because animal drug discrimination studies often use Δ^9 -THC as the standard for establishing if new drugs have classic marijuana-like pharmacological activity, HHS did not examine whether this method should be applied when evaluating the abuse potential of Δ^9 -THC. HHS Basis for Rec. at 14.

C. Human Behavioral and Physiological Effects

Subjective Effects of Δ^9 -THC

The psychological, behavioral, and subjective responses to marijuana in humans have been known and characterized since antiquity. In the modern period, data on the psychological, behavioral, and subjective responses to marijuana are available from the drug labels of FDA-approved drug products, from prospective human abuse potential (“HAP”) studies, from accounts published in the scientific and medical literature, and from an evaluation published in 2017 by the National Academies of Science, Engineering, and Medicine (“NASEM”). HHS Basis for Rec. at 14.

FDA-Approved Drug Products Containing Δ^9 -THC

Clinical scientific studies investigated the effects of Δ^9 -THC on humans during the development of the FDA-approved drug product Marinol, which contains 2.5, 5, and 10 mg dronabinol ((–)-*trans*- Δ^9 -THC of synthetic origin in sesame seed oil). During controlled clinical

trials (as reported in section 6.1 of the drug labels for Marinol and Syndros (which relied on the safety data from Marinol during drug development)), various adverse events (“AEs”) were observed, including amnesia, anxiety/nervousness, ataxia, confusion, depersonalization, hallucination, asthenia, palpitations, tachycardia, vasodilation/facial flush, euphoria, paranoid reaction, somnolence, abnormal thinking, dizziness, abdominal pain, nausea, and vomiting. HHS Basis for Rec. at 14–15.

HAP Studies

HAP studies evaluate whether a test drug produces positive subjective responses compared to a placebo and a known drug of abuse that is scheduled under the CSA and serves as the positive control. If the test drug produces rewarding effects that are statistically significantly greater than the placebo, and beyond the acceptable placebo range of response, it is an indication that the drug may have abuse potential. The relative abuse potential is suggested by the responses from the positive control on these measures in comparison to the test drug. HHS Basis for Rec. at 15.

After analyzing a number of HAP studies of marijuana and Δ^9 -THC, which varied in the dose of Δ^9 -THC, the route of administration, or whether the Δ^9 -THC was provided in the form of marijuana or isolated compound, HHS identified a number of commonalities. First, following administration of the study drug (*i.e.*, marijuana or Δ^9 -THC), there were increases in positive subjective responses. Second, the studies demonstrated increases on the Addiction Research Center Inventory scales for the morphine benzedrine group (euphoria), marijuana, and amphetamine. HHS concluded that these data consistently demonstrated that Δ^9 -THC, in the form of marijuana or as an isolated compound, produces rewarding effects that are indicative of abuse potential when it is administered under controlled experimental conditions. Third, and in contrast to the prior findings, the data also demonstrated that the administration of marijuana or Δ^9 -THC may result in negative subjective responses reflecting negative drug effects and sedation; these are often delayed in onset from when the positive subjective effects begin. HHS noted that the positive and negative subjective responses following administration of marijuana or Δ^9 -THC were often dose-dependent. It also noted that there were typically few differences between responses to marijuana and Δ^9 -THC, or between responses based on

route of administration of the study drug. HHS Basis for Rec. at 15.

Common Responses to Marijuana in Humans Published in Scientific and Medical Literature

HHS concluded that the responses to dronabinol reported during development of Marinol and the responses to marijuana and Δ^9 -THC reported in HAP studies paralleled the common responses to marijuana that have been described by other medical scientists. These responses include positive subjective responses (such as euphoria or happiness), sedative responses (such as drowsiness or changes in sleep), anxiety and negative responses (such as panic attacks, agitation, and paranoia), perceptual changes (such as hallucinations and changes in perception), psychiatric, social, and cognitive changes (such as drug abuse, delusions, memory and concentration impairment, and impaired judgment), and physiological responses (such as nausea, tachycardia, facial flushing, dry mouth, tremor, dizziness, ataxia, and hyperemesis). The literature reviewed by HHS also concluded that the positive changes that occur following use of marijuana are pleasurable to many humans and are associated with drug-seeking and drug-taking; and that these effects are typically dose-dependent, with higher doses and routes of administration that produce faster onset producing more intense responses and the likelihood of more negative subjective effects. HHS Basis for Rec. at 16–17.

National Academies of Science, Engineering, and Medicine (NASEM)

HHS also reviewed a book-length evaluation of marijuana by NASEM entitled *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*.¹⁷ According to HHS, in this evaluation, NASEM provided a brief summary of the clinical features of marijuana intoxication and found that (1) during acute cannabis intoxication, the user's sociability and sensitivity to certain stimuli (*e.g.*, colors, music) may be enhanced, the perception of time is altered, and the appetite for sweet and fatty foods is heightened; (2) some users report feeling relaxed or experiencing a pleasurable rush or buzz after smoking cannabis; (3) these subjective effects were often associated with decreased short-term memory, dry mouth, and

impaired perception and motor skills; and (4) when very high blood levels of Δ^9 -THC were attained, persons might experience panic attacks, paranoid thoughts, and hallucinations. HHS Basis for Rec. at 17–18.

HHS Conclusion With Respect to Factor 2

Based on its analysis of the studies discussed above, HHS concluded that Δ^9 -THC, the substance largely responsible for the abuse potential of marijuana, is a partial agonist at the cannabinoid CB₁ receptor. When Δ^9 -THC is administered to animals, it produces rewarding responses, as evidenced by its ability to induce self-administration and CPP. This is consistent with the data from human studies and from clinical observations, where administration of Δ^9 -THC or use of marijuana produces euphoria and other pleasurable responses, as well as sedation and anxiety responses. Psychiatric, social, and cognitive responses, which are often experienced as negative, are also reported, as are physiological responses such as dry mouth, ataxia, and increased hunger. As described in HHS's analysis of Factor 4, *see* HHS Basis for Rec. at 32–37, the rewarding responses observed in humans are consistent with the prevalence of nonmedical use of marijuana, which includes abuse of the substance. Abuse of marijuana by individuals can lead to other negative consequences, including addiction and the need to seek medical attention through calls to poison centers or visits to an ED, as described in Factor 5, *see* HHS Basis for Rec. at 38–39, 42. HHS Basis for Rec. at 18.

DEA believes that additional data on marijuana's pharmacological effects may be appropriate for consideration in assessing this factor.

3. The State of Current Scientific Knowledge Regarding Marijuana

The third factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the state of current scientific knowledge regarding marijuana. In considering this factor and making its recommendation, HHS examined the chemistry of marijuana and the human pharmacokinetics of marijuana. HHS Basis for Rec. at 18–24.

Chemistry

Cannabis is a genus of annual flowering plant with digitate leaves in the family *Cannabaceae* Martinov that likely originated in Central or Southeast Asia over 10,000 years ago and was first cultivated in China for fiber and seed production. Cultivation eventually

¹⁷ National Academies of Science, Engineering, & Medicine, *The Health Effects of Cannabis & Cannabinoids: The Current State of Evidence & Recommendations for Research* (2017), <https://nap.nationalacademies.org/read/24625/chapter/1>.

spread across Asia, Africa, and Europe and then to the Americas. A longstanding and significant historical debate by botanists and taxonomists continues today regarding the number of species in the *Cannabis* genus, but it is generally treated as a single, highly polymorphic species known as *Cannabis sativa* L., with the other two previously reported species listed as *Cannabis indica* Lam. and *Cannabis ruderalis* Janisch. Plants previously believed to be part of the latter two species are generally recognized as varieties (or subspecies) of *Cannabis sativa* L., which are commonly referred to as *sativa* var. *indica* and *sativa* var. *ruderalis*. *Cannabis sativa* and *sativa* var. *indica* plants are widely cultivated for their size, branching, and cannabinoid content, while *sativa* var. *ruderalis* is rarely cultivated alone because it is shorter, is often unbranched, and has very low cannabinoid content. Worldwide *Cannabis* varieties are separated into hundreds of different cultivars and strains. Plants selected for cultivation are known as cultivated varieties or cultivars, whereas plants reproduced asexually from a cultivar through clonal propagation are known as strains. These practices have resulted in significantly different chemical profiles for *Cannabis* cultivars, and the classification term to account for these chemical profile differences has evolved. The term “chemovar” accounts for the plant’s chemical profile and is a more meaningful classification for clinical researchers studying the plant’s potential drug effects. Marijuana products developed from diverse chemovars will have different safety, biological, pharmacological, and toxicological profiles. HHS Basis for Rec. at 18–19.

Cannabis is a dioecious plant, meaning female and male flowers occur on separate plants, and rarely occurs as a monoecious plant (*i.e.*, single plant containing male and female flowers). The glandular trichomes found on the female plant’s unfertilized flower heads and bracts contain the highest concentrations of cannabinoids. For this reason, unfertilized female chemovars are favored to harvest large inflorescences (*i.e.*, complete flower head) for their rich cannabinoid and terpene content. HHS Basis for Rec. at 19.

The *Cannabis sativa* L. plant naturally contains many different compounds, and more than 550 have been identified, such as cannabinoids, terpenoids, flavonoids, stilbenoids, steroids, polysaccharides, benzoquinone, phenanthrenes, spiroindans, lignans,

fatty acids, sugars, hydrocarbons, amino acids, and proteins. Cannabinoids are mainly found in living *Cannabis sativa* L. plants in their non-psychoactive carboxylated forms (*i.e.*, acid form), which require drying, heating, combustion, or aging to decarboxylate to their neutral forms, and are primarily composed of C₂₁ terpenophenolic compounds. The most abundant neutral form cannabinoids are Δ9-THC and CBD, but nearly 200 have been identified in the plant and are divided into subclasses: cannabigerols, cannabichromenes, CBDs, Δ9-THCs, (-)-Δ8-*trans*-tetrahydrocannabinols (“Δ8-THCs”), cannabicyclols, cannabielsoins, cannabinols, cannabinodiols, cannabitrils, and the miscellaneous cannabinoids. HHS Basis for Rec. at 19.

Like any other botanical substance, marijuana plants are heterogeneous in nature and contain a complex chemical profile. Moreover, variable organic plant material, as well as manufactured preparations, result in a variety of product forms that dictate different routes of administration, associated risks, and differences in quality of the product used, which may also influence risk for users. Among other things, these differences can result from differences in harvest location, growing conditions, the season in which the marijuana is harvested, and the manner in which the marijuana is processed, handled, transported, and tested. The potential for high variability of marijuana and marijuana-derived products, both in product composition and impurity profile, is a major consideration for the potential variability of drug effects and safety. HHS Basis for Rec. at 19–20.

Processing of marijuana and its use in further manufacturing can lead to a range of forms that individuals may use or consume, including crude mixtures and highly purified substances of botanical origin, many of which may be cannabinoid compounds. Among known cannabinoids in the *Cannabis* plant, both Δ9-THC and Δ8-THC produce marijuana’s psychoactive effects. Because Δ9-THC is significantly more abundant than Δ8-THC, marijuana’s intoxicating effects are largely attributed to the former. Only small quantities of Δ8-THC acid and Δ8-THC have been identified in plants. HHS Basis for Rec. at 20.

As noted above, the 2018 amendments to the CSA removed hemp from the definition of marijuana. However, the term “cannabis” is still often broadly used to refer to a wide variety of products manufactured from the *Cannabis sativa* L. plant, regardless of their control status. As a result of the 2018 amendments to the CSA, a large

hemp marketplace exists, containing a wide variety of products. In addition, the public has access to cannabis products within the CSA definition of marijuana through State-authorized adult-use (*i.e.*, nonmedical use) and medical-use programs, as well as via the illicit marketplace. See HHS Basis for Rec. at 28–37 (Factor 4). Because of these diverse sources of marijuana, there is a lack of unified controls on cultivation and manufacturing, which raises concerns related to the safety, quality, and consistency of botanical substances (*e.g.*, botanical raw materials, extracts, and intermediates) and final product formulations that are currently accessed for medical and nonmedical use. Products sourced from State-authorized adult-use and medical-use programs are subject to a patchwork of inconsistent product standards and safety requirements. Although some State programs have a set of standards (for example, on manufacturing, testing, labeling, and packaging), each program’s controls are different, leading to a wide variation of products across State-authorized programs. And the illicit marketplace is not subject to any standards or oversight. As a result, the range of products within the CSA’s definition of marijuana encompasses a large degree of variation in forms for consumption, composition of biologically relevant constituents, potency, and contaminants. HHS Basis for Rec. at 21.

In short, marijuana has hundreds of chemovars containing variable concentrations of Δ9-THC, cannabinoids, and other compounds. As a result, in evaluating whether to recommend that marijuana be rescheduled, HHS focused to the greatest extent possible on wide-ranging substances derived from cannabis plants that are vehicles for the self-administration of Δ9-THC as the key biologically active substance on which the CSA’s current definition of marijuana is based. HHS Basis for Rec. at 21.

Human Pharmacokinetics of Δ9-THC

HHS reported that the pharmacokinetics of Δ9-THC in humans—*i.e.*, the study of how the body interacts with Δ9-THC—have been evaluated following inhaled administration of marijuana and oral administration of marijuana. These are the most frequently used routes of administration for marijuana or isolated Δ9-THC. HHS Basis for Rec. at 21.

Marijuana is commonly administered by humans via inhalation through smoking and, more recently, through vaping (*e.g.*, heating and inhalation of

botanical matter or other volatile substances containing $\Delta 9$ -THC). Generally, inhalation of a drug is the route that produces the fastest rate of drug absorption. Once marijuana is inhaled, $\Delta 9$ -THC is absorbed through the lungs in the form of an aerosol within seconds. Peak plasma levels of $\Delta 9$ -THC following inhalation occur very quickly, within 6 to 10 minutes. Psychoactive effects begin immediately following absorption, although peak subjective effects do not coincide with peak plasma $\Delta 9$ -THC levels and are often delayed. Following administration of marijuana through inhalation, the bioavailability of $\Delta 9$ -THC is 10 percent to 35 percent. That bioavailability is relatively low and varies widely due to several factors. An individual's experience and technique with smoking marijuana also determines the dose absorbed. HHS Basis for Rec. at 22.

When marijuana or $\Delta 9$ -THC is administered orally (such as by eating marijuana-infused foods), the effects start within 30 to 90 minutes, reach their peak at 1.5 to 3 hours, and remain measurable for 4 to 12 hours. Oral bioavailability of $\Delta 9$ -THC, following ingestion of an edible containing marijuana or isolated $\Delta 9$ -THC, ranges from 5 to 20 percent. The low and variable bioavailability of $\Delta 9$ -THC from oral ingestion is a consequence of its first-pass hepatic elimination from blood and erratic absorption from stomach and bowel. Ingestion of brownies containing marijuana also results in lower $\Delta 9$ -THC plasma levels relative to inhalation of marijuana. HHS Basis for Rec. at 22–23.

Although there are differences in absorption of $\Delta 9$ -THC depending on route of administration, the distribution, metabolism, and excretion of $\Delta 9$ -THC is similar regardless of how the drug is administered. Plasma concentrations of $\Delta 9$ -THC decrease quickly after absorption through rapid distribution into tissues and through liver metabolism. Because $\Delta 9$ -THC has high lipophilicity, the apparent volume of distribution of $\Delta 9$ -THC is high (10 L/kg) as it is distributed initially into organs such as lung, heart, brain, and liver that are highly perfused. Over time with regular exposure to marijuana, $\Delta 9$ -THC will concentrate and be retained in fat. HHS Basis for Rec. at 23.

Metabolism of $\Delta 9$ -THC occurs primarily via cytochrome P450 isozymes (CYP2C9, CYP2C19, and CYP3A4) via microsomal hydroxylation to both active and inactive metabolites. The primary active metabolite of $\Delta 9$ -THC is 11-hydroxy- $\Delta 9$ -THC. $\Delta 9$ -THC clears from the blood relatively rapidly, largely because it is redistributed to

other tissues in the body. Metabolism of $\Delta 9$ -THC in most tissues is relatively slow or absent. The majority of the absorbed $\Delta 9$ -THC dose is eliminated in feces, and about 33 percent in urine. HHS Basis for Rec. at 23.

HHS Conclusion With Respect to Factor 3

In conclusion, HHS found that the pharmacokinetic profile of marijuana varies greatly depending on route of administration. Inhalation of marijuana produces a rapid increase in plasma levels of $\Delta 9$ -THC and an immediate onset of psychological effects. In comparison, oral administration of marijuana produces a much slower increase in plasma levels of $\Delta 9$ -THC and onset of psychological effects. Once $\Delta 9$ -THC has been absorbed, however, the metabolism and excretion of $\Delta 9$ -THC follows a standard path. HHS Basis for Rec. at 24.

DEA likewise notes that there is considerable variability in the cannabinoid concentrations and chemical constituency among marijuana samples and that the interpretation of clinical data related to marijuana is complicated. A primary issue is the lack of consistent concentrations of $\Delta 9$ -THC and other substances in marijuana, which complicates the interpretation of the effects of different marijuana constituents. Additionally, the non-cannabinoid components in marijuana may potentially modify the overall pharmacological and toxicological properties of various marijuana strains and products. DEA anticipates that additional data on other marijuana constituents, routes of administration of marijuana, and the impact on $\Delta 9$ -THC potency may be appropriate for consideration.

4. Marijuana's History and Current Pattern of Abuse

The fourth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is marijuana's history and current pattern of abuse, which can include its abuse relative to relevant comparator substances that are abused. See HHS Basis for Rec. at 28–37. HHS concluded that it is appropriate to consider the Federal- and State-level history of marijuana control, marijuana sources for nonmedical and medical use, marijuana use in the United States since passage of the CSA, and current patterns of use and abuse of marijuana. HHS Basis for Rec. at 28.

Federal History of Marijuana Control

According to HHS, marijuana was described in the United States

Pharmacopoeia¹⁸ as early as 1850. Around the time that Congress passed the Pure Food and Drug Act of 1906, Public Law 59–384, 34 Stat. 768, drugs such as marijuana, alcohol, heroin, morphine, and cocaine began to be characterized by the Federal Government as addictive and dangerous. These drugs were frequently included in patent medicines, often without the consumer's knowledge. The 1906 law required accurate drug labeling with respect to ingredients and dosage. But it did not prohibit the sale or possession of drugs characterized as addictive and dangerous drugs, including marijuana. As nonmedical use of marijuana and opioids became more popular in the United States, Congress provided funding in 1929 for two “narcotic farms” in Lexington, Kentucky, and Fort Worth, Texas, which were medical treatment centers run by the Public Health Service for federal prisoners who were “habitual users of narcotics,” including marijuana-derived products. HHS Basis for Rec. at 28–29.

In the first half of the twentieth century, marijuana use was curbed by several Federal laws. In 1931, the importation of marijuana into the United States began to be restricted under regulations under the Pure Food and Drug Act, except for medicinal purposes. The Marihuana Tax Act of 1937, Public Law 75–238, 50 Stat. 551, imposed taxes that effectively prohibited marijuana use for medical, nonmedical, scientific, or industrial purposes. Five years later, in 1942, marijuana was removed from the United States Pharmacopoeia. Through the imposition of mandatory minimums, the Boggs Act of 1951, Public Law 82–255, 65 Stat. 767, lengthened the average sentence for first time marijuana offenders to 2 to 5 years, similar to that for opioid offenses, regardless of whether the individual was a nonmedical user or a trafficker. The Narcotic Control Act of 1956, Public Law 84–728, 70 Stat. 567, increased the minimum sentence for a first offender for marijuana to 2 to 10 years. HHS Basis for Rec. at 29.

Despite the legal consequences, nonmedical marijuana use increased dramatically in the 1960s, especially among youth. Congress passed the CSA in 1970. The CSA effectively repealed

¹⁸ The United States Pharmacopoeia was formed as an “independent, scientific, non-profit organization dedicated to public health” that published “a national, uniform set of guidelines for the best understood medicinal substances and preparations of the day.” *Building Trust for Over 200 Years: A Timeline of USP, U.S. Pharmacopoeia*, <https://www.usp.org/200-anniversary/usp-timeline> (last visited May 11, 2024).

all previous Federal drug laws, including the Marihuana Tax Act, and provided a unified framework for control of drugs with abuse potential. When the CSA was enacted, marijuana was placed into schedule I, which prohibited use of marijuana for medicinal or nonmedical purposes other than legitimate scientific research and analysis. This placement was consistent with the criteria established by the CSA under 21 U.S.C. 812. HHS Basis for Rec. at 29–30.

Marijuana Control at the State Level

According to HHS, changes in State-level marijuana laws in the United States in the modern era began in 1996 with the approval of Proposition 215, the Compassionate Use Act, by voters in California. This law legalized the use, possession, and cultivation of marijuana for treatment of patients with cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief, when recommended by a physician. Under the law, marijuana could also be cultivated by patient caregivers. HHS Basis for Rec. at 30.

As of August 2023, when HHS submitted its Basis for Recommendation to DEA, State-level laws allowing medicinal use of marijuana had been passed in a total of 38 States, plus the District of Columbia: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Hawaii, Illinois, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Utah, Vermont, Virginia, Washington, and West Virginia. Medical use of marijuana was legalized through the action of 20 State legislatures and by 18 ballot measures.¹⁹ HHS Basis for Rec. at 30.

In 2012, Colorado and Washington became the first States to legalize the nonmedical use of marijuana. As of August 2023, State-level legalization of the nonmedical use of marijuana has occurred in a total of 23 States and the District of Columbia: Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri,

Montana, Nevada, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Virginia, and Washington. Nonmedical use of marijuana was legalized by ballot initiatives in 13 States and by State legislatures in 9 States. HHS Basis for Rec. at 30.

Marijuana Use in the United States Since Passage of the CSA

Marijuana use has varied since the CSA was passed in 1970. Gallup Poll data from 1969 to 2013 show a steady increase over time in affirmative responses to whether the respondent had personally tried marijuana, with only 4 percent of people saying they had tried marijuana in 1969 compared to 38 percent in 2013. As HHS observed, the 2017 NASEM report stated that the prevalence of marijuana use peaked in the late 1970s, declined through the 1980s, and then increased again in the mid-1990s. From 2007 to 2017, there were steady year-over-year increases in the share of the general population that used marijuana in the past month, although there is no clear explanation for the post-2007 increase in use rates. HHS Basis for Rec. at 31–32.

Current Patterns of Use and Abuse of Marijuana

In considering current patterns of use and abuse of marijuana and marijuana-derived products, HHS analyzed epidemiological databases from 2015 to the most recent years of available data (which vary among data sources). A wide variety of epidemiological databases provide necessary data for HHS's analyses. These include the NSDUH; Behavioral Risk Factor Surveillance System ("BRFSS"); Research Abuse, Diversion and Addiction-Related Surveillance ("RADARS"); Nonmedical Use of Prescription Drugs ("NMURx"); Monitoring the Future ("MTF"); Youth Risk Behavioral Surveillance System ("YRBSS"); and International Cannabis Policy Study ("ICPS"). HHS Basis for Rec. at 32.

National Survey on Drug Use and Health

Based on NSDUH data, HHS concluded that from 2015 to 2019 the past-year use of marijuana for any reason (nonmedical and medical) among people ages 12 years and older increased from 14 percent to 18 percent. By contrast, past-year (nonmedical and medical) use of comparator drugs that have FDA-approved therapeutic indications declined or remained relatively stable over the same timeframe, including hydrocodone (22

percent to 16 percent), benzodiazepines (12 percent to 11 percent, 2017 to 2019 only), oxycodone (11 percent to 9 percent), tramadol (7 percent to 6 percent), zolpidem (4 percent to 3 percent), and ketamine (less than 1 percent). Although there were trend breaks for the years 2020 and 2021,²⁰ marijuana past-year use continued to increase during these two years. HHS Basis for Rec. at 32–33.

Based on NSDUH data, HHS concluded that from 2015 to 2019, the prevalence of past-year nonmedical use of marijuana (*i.e.*, use without a health care provider ("HCP") recommendation) among people ages 12 years and older also increased. HHS's finding was based on an increase in the prevalence of overall nonmedical use of marijuana from 12 percent to 15 percent and on an increase in nonmedical use of marijuana only, without nonmedical use of other drugs that are abused, from 8 percent to 11 percent during this period. There was a slight decrease in both categories in 2020, but the prevalence of both kinds of uses increased again in 2021 (to 16 percent and 11 percent, respectively) to levels that were higher than those reported in 2019. In contrast, the prevalence of past-year nonmedical use of comparator drugs was less than 3 percent for heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem, which is much less than that for marijuana, either alone or with other drugs. Over the 2015 to 2021 reporting period, the overall use of these comparator drugs declined slightly or remained fairly stable. Notably, the majority of individuals who reported nonmedical use of marijuana did not report nonmedical use of the comparator drugs. And over the same reporting period of 2015 to 2021, the prevalence of past-year use of alcohol ranged from 62 percent to 65 percent for individuals ages 12 years and older, far exceeding the prevalence for marijuana or other comparator drugs. These data demonstrate that alcohol has the highest prevalence of past-year-only use, followed by nonmedical use of marijuana. The prevalence of the other comparators is far below that of alcohol and marijuana. HHS Basis for Rec. at 33.

HHS also concluded that the NSDUH data show that most individuals who used marijuana in the past year did not do so based on a recommendation from an HCP, but marijuana use was more frequent among users with an HCP

¹⁹ Data on the number of patients who participate in State-sanctioned medical cannabis use is available here: *Medical Cannabis Patient Numbers, Marijuana Pol'y Project*, <https://www.mpp.org/issues/medical-marijuana/state-by-state-medical-marijuana-laws/medical-marijuana-patient-numbers> (last visited May 13, 2024).

²⁰ HHS noted that NSDUH data collection was disrupted in 2020 and 2021 due to the COVID-19 pandemic, leading to trend breaks in these years. HHS Basis for Rec. at 32.

recommendation. The yearly percentage of individuals who used marijuana but did not have an HCP recommendation ranged between 84 and 89 percent between 2015 and 2021; by comparison, exclusive medical use of marijuana that was recommended by an HCP ranged between 7 and 10 percent of marijuana users in the same period. According to HHS, approximately 50 percent of those individuals without an HCP recommendation used marijuana for 60 or fewer days in the year, while 29 percent used marijuana for more than 241 days in the year. In contrast, for those individuals whose use of marijuana was sometimes or always recommended by an HCP, 51 percent and 55 percent (respectively) used marijuana at least 241 days in the year. HHS Basis for Rec. at 33–34.

The NSDUH data from 2021 showed that among individuals who used any marijuana in the past year, 69 percent used marijuana in the prior month. For comparator drugs, the percentage of individuals with past-year use who used each substance nonmedically in the past month was 76 percent for alcohol, 49 percent for heroin, 38 percent for cocaine, and 28 percent for ketamine. HHS Basis for Rec. at 34.

Behavioral Risk Factor Surveillance System

BRFSS is a national, State-based, cross-sectional telephone survey conducted by the Centers for Disease Control and Prevention (“CDC”). The participants in the 2021 BRFSS module for marijuana included approximately 68 million individuals 18 years and older, residing in 24 States and Territories: Alaska, Connecticut, Delaware, Hawaii, Idaho, Illinois, Indiana, Kentucky, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New York, North Dakota, Ohio, Oklahoma, Rhode Island, Utah, Vermont, Wyoming, and Guam. HHS Basis for Rec. at 34.

For the 2021 survey year, the estimated prevalence of past-month marijuana use for any reason in the BRFSS survey was 12 percent, with 88 percent reporting no marijuana use. Among those with past-month marijuana use, the mean frequency of use was 17 days per month, with half of respondents reporting that they used marijuana 20 to 30 days per month. This pattern was consistent across all age and sex categories. HHS Basis for Rec. at 34.

When the reason for use was evaluated, the percentage of individuals who reported use for both medical and nonmedical reasons was 39 percent, compared to 36 percent for those who reported use for nonmedical reasons

only, and 25 percent for those who reported use for medical reasons only. Those individuals who reported past-month use of marijuana for medical reasons were more likely to be adults 55 years and older, while individuals who reported past-month marijuana use for nonmedical reasons only were more likely to be younger adults aged 18 to 24 years. HHS Basis for Rec. at 34.

Individuals who reported using marijuana in the past 30 days for both nonmedical and medical reasons were more likely (62 percent) to report marijuana use near daily (20 to 30 days per month) than individuals who reported marijuana use for nonmedical reasons only (34 percent). Similarly, individuals who used marijuana for medical reasons only were also more likely (57 percent) to report near daily use than those who used it for nonmedical reasons only. HHS Basis for Rec. at 34.

Researched Abuse, Diversion and Addiction-Related Surveillance System Survey of Nonmedical Use of Prescription Drugs

The RADARS System conducts the NMURx Program, a serial, cross-sectional, online survey of the general adult population (18 years and older) to elicit information on the nonmedical use of drugs (prescription, nonprescription, unapproved, and illicit). The NMURx Program estimates represent measures of past-year drug use in an enriched sample of United States adults with higher-than-average nonmedical use of prescription pain relievers and illicit drugs. NMURx program data demonstrated that past-year use of marijuana was reported by 21 percent of individuals, while past-year use of comparator substances was substantially lower: benzodiazepines (4 percent), hydrocodone, oxycodone, tramadol (2 percent), cocaine or crack (less than 2 percent), and illicit fentanyl, heroin, and ketamine (less than 1 percent). This pattern of much greater marijuana use compared to other drugs is consistent with the patterns reported in NSDUH and BRFSS. HHS Basis for Rec. at 35.

Monitoring the Future

MTF collects information on the use of selected prescription and illicit drugs and alcohol by conducting an annual, nationally representative, cross-sectional survey of 8th, 10th, and 12th graders in public and private schools.²¹ MTF data showed that during the years

²¹ As a result of the COVID–19 pandemic, there is a potential trend break in the 2020 MTF data. HHS Basis for Rec. at 35.

2012 to 2022, the illicit drug most frequently used by 12th-grade students who reported past-year drug use was marijuana/hashish (approximately 35 percent per year from 2012 to 2020, with a reduction to 30 percent per year in 2021 and 2022). In contrast, in 2022, alcohol was used by 52 percent of 12th-grade students within the last 12 months, similar to percentages in 2019 and 2020 (52 percent and 55 percent, respectively), but higher than the 2021 level of 47 percent. All other comparator drugs (hydrocodone, heroin, tramadol, cocaine, ketamine, and zolpidem) were each used in the past year by fewer than 5 percent of 12th graders from 2012 to 2022. HHS Basis for Rec. at 35.

MTF data for past-month use showed a similar pattern. During the years 2012 to 2022, the illicit drug most frequently used by 12th-grade students who reported past-month drug use was marijuana/hashish (approximately 20 to 22 percent per year) compared to past-month use of cocaine (approximately 1 percent per year) or heroin (less than 0.5 percent per year). However, past-month alcohol use by 12th-grade students (28 percent) exceeded that of marijuana in 2022. For those who used marijuana in the past month, 6 to 7 percent used it daily. By comparison, for those who used cocaine and heroin in the last month, less than one percent used it daily. MTF does not provide past-month use data for hydrocodone, heroin, tramadol, ketamine, or zolpidem. HHS Basis for Rec. at 35.

Youth Risk Behavior Surveillance System

YRBSS was established by the CDC and conducts school-based surveys every 2 years, in partnership with State, local, Territorial, and Tribal governments, with a focus on youth health behavior in the United States. The YRBSS high school component, the Youth Risk Behavior Survey, includes a nationally representative survey of 9th-through 12th-grade students. YRBSS data showed that from 2009 to 2019, approximately 20 percent of students in 9th through 12th grade reported using marijuana at least once in the past month during each year evaluated. When students 17 years and older were asked how old they were when they first used marijuana, 43 percent reported they initiated use between the ages of 15 to 16 years, 25 percent initiated use between the ages of 13 to 14 years, and 13 percent initiated use at 12 years of age and younger. YRBSS data also showed, however, that past-month alcohol use by high school students (29 percent) in 2019 was greater than that of marijuana use, while past month

prescription opioid misuse (including codeine, hydrocodone, or oxycodone) (7 percent) in 2019 was much lower than that of both alcohol and marijuana use. HHS Basis for Rec. at 36.

International Cannabis Policy Study

ICPS conducted serial, cross-sectional surveys from 2019 to 2021 of individuals ages 16 to 65 years living in the United States to understand the public health impact of marijuana legalization. HHS's evaluation of that survey data focused on respondents who reported at least some past-year marijuana nonmedical use (by indicating that they were not a medical marijuana user, defined as someone who uses marijuana only to treat a medical condition). HHS Basis for Rec. at 36.

According to HHS, ICPS data showed that the prevalence of past-year nonmedical use of marijuana ranged from 18 percent to 22 percent of individuals surveyed from 2019 to 2021, while the prevalence of past-month nonmedical use was lower, ranging from 12 percent to 14 percent of individuals surveyed. Individuals aged 26 to 34 years had the highest relative prevalence of nonmedical marijuana use, with 26 percent reporting past-year use and 18 percent reporting past-month use. When those individuals who reported past-year marijuana use in 2021 were asked why they used the drug, 33 percent reported use for medical reasons, while 61 percent were classified as using marijuana for nonmedical reasons only. (The other 6 percent did not respond.) HHS Basis for Rec. at 36.

When frequency of nonmedical use of marijuana was evaluated in ICPS for those individuals who used marijuana nonmedically at least once a year, individuals aged 16 to 17 years had the highest percentage of use less than once a month (approximately 40 percent, compared to approximately 25 to 31 percent for other age cohorts); while individuals aged 26 to 34 years had the highest percentage of daily use (approximately 43 percent, compared to approximately 34 to 37 percent for individuals in other adult cohorts and approximately 24 percent among individuals 16 and 17 years). Among individuals who used marijuana for nonmedical reasons in the past year, 49 percent reported never using alcohol and marijuana at the same time, while 35 percent sometimes used the two substances together, 9 percent often used them together, and 5 percent used alcohol every time they used marijuana. HHS Basis for Rec. at 36–37.

HHS Conclusion With Respect to Factor 4

In light of the evidence cited above, HHS determined that certain conclusions could be drawn about marijuana's current pattern of abuse. HHS concluded that the use of marijuana for medical and nonmedical purposes is extensive in the United States. HHS also concluded that the prevalence of marijuana use is less than that of alcohol and significantly more than that of other drugs of abuse that are scheduled under the CSA. Specifically, HHS noted that NSDUH data from 2015 to 2019 showed that the prevalence of past-year use of alcohol was five to six times greater than that of nonmedical use of marijuana. In contrast, the prevalence of past-year nonmedical use of heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem was four to five times less than that of marijuana nonmedical use. Similar past-year comparative drug use data were reported in RADARS–NMURx, MTF, and ICPS. HHS Basis for Rec. at 37. In 2016, DEA found that marijuana continues to be the most widely used illicit drug. It noted that in 2014, there were 22.2 million current users; that there were also 2.6 million new users, most of whom were less than 18 years of age; and that marijuana was the most frequently identified drug identified in Federal, State, and local forensic laboratories. 81 FR 53739. In addition to the data provided in the HHS Basis for Recommendation and the data considered by HHS and DEA in their 2015 eight-factor analyses, DEA anticipates that additional information arising from this rulemaking will further inform the findings that must be made to reschedule marijuana, including with respect to this factor. DEA also notes that, according to the World Health Organization, cannabis is globally the most commonly used psychoactive substance under international control.²² Accounting for half of all drug seizures worldwide, the global annual prevalence of cannabis consumption is 2.5 percent or about 147 million people.²³ In 2016, an estimated 28.6 million individuals age 12 or older were current (in the past month) illicit drug

users.²⁴ By 2020, approximately 59.3 million individuals age 12 or older reported using an illicit drug within the past year; 83.6 percent (49.6 million) of those past-year illicit drug users reported using marijuana.²⁵ In 2022, the Domestic Cannabis Eradication and Suppression Program was responsible for the eradication of 4,435,859 illegally cultivated outdoor cannabis plants and 1,245,980 illegally cultivated indoor plants for a total of 5,681,839 illegally cultivated marijuana plants.²⁶ DEA believes that additional data on marijuana's pattern of abuse may be appropriate for consideration in assessing this factor.

5. The Scope, Duration, and Significance of Abuse

The fifth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the scope, duration, and significance of marijuana abuse. In conducting its analysis, HHS analyzed the consequences over time of marijuana abuse compared to the abuse of other substances based on data from the United States Poison Centers National Poison Data System (“NPDS”), NSDUH, the Treatment Episode Data Set (“TEDS”), the National Addictions Vigilance Intervention and Prevention Program (“NAVIPPRO”), the National Emergency Department Sample (“NEDS”), the National Inpatient Sample (“NIS”), and the National Forensic Laboratory Information System (“NFLIS”). HHS Basis for Rec. at 37–45.

Epidemiological Data on Consequences of Marijuana Abuse

National Poison Data System

Data from NPDS provide information on the scope of contacts with a poison center (“PC”) following marijuana abuse relative to abuse of selected comparators. HHS Basis for Rec. at 38.

The number of PC abuse cases for a substance (either alone or in combination with another substance) for the period of 2015 to 2021 showed that the highest number of PC abuse cases was for alcohol, followed by heroin and

²⁴ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health 1* (2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>.

²⁵ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health 2* (2021), <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFR1PDWHTMLFiles2020/2020NSDUHFFR1PDW102121.pdf>.

²⁶ Domestic Cannabis Suppression/Eradication Program, DEA, <https://www.dea.gov/operations/eradication-program> (last visited May 13, 2024).

²² World Health Org., *The Health and Social Effects of Nonmedical Cannabis Use*, at v (2016), <https://iris.who.int/bitstream/handle/10665/251056/9789241510240-eng.pdf>.

²³ Alcohol, Drugs & Addictive Behaviours Unit, Cannabis, World Health Org., <https://www.who.int/teams/mental-health-and-substance-use/alcohol-drugs-and-addictive-behaviours/drugs-psychoactive/cannabis> (last visited May 13, 2024).

then benzodiazepines. The fourth highest number of PC abuse cases was for marijuana, with all other comparators showing fewer PC abuse cases. When the PC abuse cases for 2015 to 2021 were analyzed for cases involving a single substance only, the rank order of PC abuse cases by number was the same as the order from all PC abuse cases for substances used alone or in combination with another substance, meaning that marijuana accounted for the fourth highest number of PC abuse cases for a single substance. HHS Basis for Rec. at 38.

HHS's analysis of the data from 2015 to 2021 showed cases resulting from abuse (as opposed to those resulting from other causes, such as accidental ingestion) made up the largest proportion of PC cases for illicit fentanyl (72 percent), heroin (65 percent), cocaine (41 percent) and ketamine (40 percent). The fifth highest percentage was for cases involving marijuana (36 percent), followed by alcohol (15 percent), oxycodone (13 percent), benzodiazepines (8 percent), hydrocodone (5 percent), tramadol (4 percent), and zolpidem (3 percent). A similar analysis for single-substance-only abuse for the same period showed that the three substances most likely to lead to a PC call following abuse were heroin (65 percent), oxycodone (47 percent), and tramadol (47 percent). The fourth highest percentage was for marijuana and ketamine (46 percent), followed by alcohol (43 percent), zolpidem (40 percent), hydrocodone (37 percent), illicit fentanyl (34 percent), benzodiazepines (32 percent), and cocaine (28 percent). HHS Basis for Rec. at 38.

Annual utilization-adjusted abuse case rates were calculated by dividing the number of PC abuse case counts by the prevalence of past-year use based on NSDUH estimates from people aged 12 years and older, for the period 2015 to 2019, for both (1) any past-year use of the substance and (2) past-year nonmedical use of the substance. These utilization-adjusted rates convey the likelihood that use of a drug will result in PC abuse cases when considering how many people use the drug for either (1) any reason or (2) nonmedical reasons. The utilization-adjusted abuse rates for any past-year use of a substance showed the highest rate for heroin (increasing from 4,038 to 7,201 cases per one million people). The next highest rates were for ketamine, cocaine, and benzodiazepines; all these rates were considerably lower than the rate for heroin. The rates for marijuana (relatively stable at 75 to 70 cases per one million people) and oxycodone

were similar, as were the rates for alcohol, zolpidem, tramadol, and hydrocodone; all these rates were considerably lower than the rates for ketamine, cocaine, and benzodiazepines. A similar pattern of utilization-adjusted abuse rates was seen among cases involving a single substance only during the same time period. HHS Basis for Rec. at 39.

An analysis of medical outcomes related to exposure based on severity, timing, and assessment of clinical effects for all single-substance PC abuse cases involving marijuana or comparator drugs showed that serious medical outcomes (moderate effect, major effect, or death) were greatest for illicit fentanyl (81 percent) and heroin (79 percent), followed by oxycodone (70 percent), ketamine (64 percent), tramadol (62 percent), cocaine (59 percent), hydrocodone (44 percent), marijuana (41 percent), benzodiazepines (32 percent), alcohol (31 percent), and zolpidem (27 percent). HHS noted that death rates are underreported in NPDS, but HHS observed that the highest death rate was for fentanyl (25 percent); cocaine, heroin, and alcohol had comparatively very low death rates (3 percent, 2 percent, and 2 percent, respectively), with all other comparators reporting death rates of less than 1 percent. HHS Basis for Rec. at 39–40.

National Survey on Drug Use and Health

Data from NSDUH provide nationally representative information on the prevalence of substance use disorder (“SUD”) in 2021 among individuals aged 12 years or older who reported nonmedical use of marijuana in past year in comparison to heroin, cocaine, or alcohol use in the past year. A diagnosis of SUD is made when an individual endorses at least 2 of the 11 criteria for SUD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (“DSM-V”). Individuals are classified with a mild SUD if they meet two to three of the criteria, a moderate SUD if they meet four to five of the criteria, and a severe SUD if they meet six or more of the criteria. HHS Basis for Rec. at 40.

NSDUH data showed that, among individuals with past-year heroin use in 2021, there was an 81 percent prevalence of meeting the criteria for a heroin SUD. In comparison, there was a 30 percent prevalence of meeting the criteria for marijuana SUD among individuals who used marijuana for nonmedical reasons only (17 percent mild, 8 percent moderate, and 5 percent severe). For individuals who used marijuana for nonmedical purposes and

did not use other drugs illicitly, there was a slightly lower prevalence (24 percent) of meeting the criteria for SUD (15 percent mild, 6 percent moderate, and 3 percent severe). For cocaine, 30 percent of individuals who used cocaine in the past year met criteria for cocaine SUD (13 percent mild, 5 percent moderate, and 12 percent severe). For individuals who used alcohol in the past year, the prevalence of alcohol SUD was 17 percent (10 percent mild, 4 percent moderate, and 3 percent severe). HHS Basis for Rec. at 40.

Although the 2021 NSDUH data showed that the likelihood of meeting the criteria for a SUD was highest for heroin, followed by marijuana, cocaine, and alcohol, the absolute number of individuals who met the criteria had a different order. Alcohol had the highest number of such individuals (approximately 29,544,000), followed by marijuana (approximately 13,078,000 people with marijuana nonmedical-only use, and approximately 7,454,000 with nonmedical-only use and no nonmedical use of other drugs), cocaine (approximately 1,408,000), and heroin (approximately 894,000). HHS Basis for Rec. at 40.

Treatment Episode Data Set

TEDS is a database run by SAMHSA within HHS that presents information on the demographic and substance use characteristics of annual admissions for treatment for alcohol and drug abuse in State-approved facilities that are required by the States to provide TEDS client-level data. Because TEDS is based only on reports from these facilities, TEDS data do not represent the total national demand for substance abuse treatment or the prevalence of substance abuse in the general population. HHS Basis for Rec. at 40–41.

Out of 1.4 million admissions documented in the 2020 TEDS dataset, the most frequently reported primary drug of admission was alcohol (31 percent, or 442,014 admissions), followed by heroin (21 percent, or 292,126 admissions), marijuana (10 percent, or 139,481 admissions), and cocaine (5 percent, or 71,725 admissions). Other comparator drugs were each reported as the primary drug in less than 2 percent of admissions. Over the reporting period of 2015 to 2020, the proportion of admissions each year ranged from 30 to 33 percent for alcohol; from 21 to 26 percent for heroin; from 10 to 14 percent for marijuana; and from 5 to 6 percent for cocaine. The proportion of admissions with marijuana as the primary drug declined each year from 14 percent in 2015 to a low of 10 percent in 2020,

while the proportion of admissions with cocaine as the primary drug increased slightly during this time from 5 percent in 2015 to 6 percent in 2019. During this reporting period, other comparator drugs were each reported as the primary drug in less than 2 percent of admissions each year. HHS Basis for Rec. at 41.

In 2020, marijuana and cocaine were most likely to be reported as the secondary drug at admission (25 percent and 24 percent, respectively), followed by alcohol (15 percent), heroin (8 percent), and benzodiazepines (6 percent), with all other comparators reported as less than 2 percent. For tertiary drugs at admission, marijuana (29 percent) was reported most frequently, followed by cocaine (18 percent), alcohol (16 percent), and heroin (5 percent), with all other comparators reported as less than 2 percent. HHS Basis for Rec. at 41.

National Addictions Vigilance Intervention and Prevention Program

NAVIPPRO is a surveillance system for substance use and nonmedical use of prescription medication in a convenience sample of adults seeking treatment or being assessed for SUD treatment at participating facilities across the United States. NAVIPPRO Addiction Severity Index-Multimedia Version (“ASI-MV”) is a clinical assessment tool that collects data on recent drug use behaviors for evaluation and treatment planning at intake. From 2020 through 2021, there were a total of 76,249 NAVIPPRO ASI-MV assessments in individuals entering or being assessed for SUD treatment at a center participating in the NAVIPPRO network. The drug most frequently endorsed for past-month use was marijuana (20,458 individuals, or 27 percent), followed by alcohol (5 or more alcoholic drinks per day, 16,388 individuals, or 22 percent), heroin (9,078 individuals, or 16 percent), fentanyl (6,186 individuals, or 8 percent), hydrocodone (3,448 individuals, or 5 percent), oxycodone (3,186 individuals, or 4 percent), cocaine or crack (5,417 individuals, or 7 percent), tramadol (543 individuals, or 1 percent), and ketamine (169 individuals, or less than 1 percent). HHS Basis for Rec. at 41.

Nationwide Emergency Department Sample

NEDS is the largest all-payer ED database in the United States, as developed for HHS’s Agency for Healthcare Research and Quality (“AHRQ”). NEDS is a sample of records from ED visits from the State Emergency

Department Databases, which capture discharge information on all ED visits that do not result in hospital admission, and the State Inpatient Databases, which contain information on patients first seen in the ED and then admitted. The 2020 ED sample covered 995 hospital EDs and 41 States; the unweighted 2020 sample contained data from over 28 million ED visits, which resulted in a weighted estimate of 123 million ED visits. HHS compared ED visits that noted an alcohol, marijuana, or cocaine-related disorder; this comparison included ED visits not directly due to a specific substance-related disorder, but in which the patient was recorded as having had an alcohol, marijuana, or cocaine-related disorder in the administrative claim associated with the visit. HHS Basis for Rec. at 42.

Based on NEDS data, from 2016 to 2020, the highest estimated number of annual ED visits was for an alcohol-related disorder, with between 4 million and 4.1 million visits each year, 3.2 million of which involved alcohol as a single substance. Over the same timeframe, estimated annual ED visits involving a marijuana-related disorder ranged from approximately 1.3 million to over 1.7 million, with the estimated annual ED visits for single-substance marijuana disorder ranging from 757,731 to 1.08 million. For cocaine, the estimated annual ED visits involving a related disorder were between 559,165 and 774,737, with annual visits for single-substance cocaine-related disorder ranging from 204,257 to 266,614. HHS Basis for Rec. at 42.

HHS calculated a utilization-adjusted rate of estimated ED visits, and the highest rate was for cocaine-related disorder, which ranged from 11,765 to 14,014 visits per 100,000 individuals, of which 4,011 to 4,952 were single-substance visits. Marijuana had the second-highest utilization-adjusted rate of estimated ED visits, ranging from 3,472 to 3,940 per 100,000 individuals 2,017 to 2,413 of which were single-substance visits. The utilization-adjusted rate of visits involving an alcohol disorder, the lowest of the three substances, ranged from 2,225 to 2,327 per 100,000 individuals, of which 1,775 to 1,843 were single-substance ED visits. HHS Basis for Rec. at 42–43.

National Inpatient Sample

NIS is the largest publicly available all-payer inpatient administrative health care database in the United States, and it is sponsored by AHRQ. It is a sample of discharges from participating community hospitals from 46 to 48 States and the District of Columbia each year, with approximately 7 million

unweighted inpatient stays annually, accounting for weighted annual estimates of 35 million hospitalizations. HHS used NIS data to compare alcohol, marijuana, and cocaine. HHS Basis for Rec. at 43.

From 2016 to 2020, alcohol-related disorder had the highest estimated annual number of hospitalizations, at approximately 1.8 million each year, of which approximately 1.2 to 1.25 million involved single-substance alcohol-related disorder. Marijuana-related disorder had the second-highest estimated annual number of hospitalizations, increasing from 795,140 in 2016 to 914,810 in 2020, of which 373,160 to 452,985 were for single-substance marijuana-related disorder. Cocaine had the lowest estimated annual number of hospitalizations, ranging from 387,385 to 453,955, of which 94,695 to 112,725 were for single-substance cocaine-related disorder. HHS Basis for Rec. at 43.

HHS then calculated a utilization-adjusted rate of estimated hospitalizations, and the highest rate was for cocaine-related disorder, which ranged from 7,185 to 8,211 hospitalizations per 100,000 individuals with any past-year use, of which 1,796 to 2,039 were single-substance hospitalizations. Marijuana-related disorder had the second-highest rate of estimated hospitalizations, ranging from 1,850 to 2,117 per 100,000 individuals, of which 906 to 1,026 were single-substance hospitalizations. Alcohol had the lowest rate, ranging from 987 to 1,039 per 100,000 individuals, of which 675 to 715 were single-substance hospitalizations. HHS Basis for Rec. at 43.

National Forensic Laboratory Information System

NFLIS is a program of the Diversion Control Division of DEA. The NFLIS-Drug system is a component of the NFLIS that contains data that serve as a surveillance resource to monitor drug encounters by law enforcement across the United States, including data on drugs seized by law enforcement and submitted to Federal, State, and local forensic laboratories for analysis. In NFLIS, a law enforcement investigation (“case”) may result in one or more “reports” or “exhibits” of drug evidence, and each report or exhibit may contain one drug or multiple drugs. However, NFLIS-Drug data has limitations because not all drugs encountered by law enforcement are sent for analysis and not all drugs sent to reporting forensic laboratories are tested. To account for nonreporting

laboratories, among other things, DEA publishes NFLIS-Drug national report estimates annually and semiannually. Analyzing national estimates data allows for a comparison of the number of reports by year and reporting trends. In calculating national and regional estimates, DEA uses all NFLIS-Drug reporting laboratories. HHS Basis for Rec. at 43–44.

In 2021, there were 1,326,205 drug reports from State and local forensic laboratories in the United States, an increase of 3 percent from 2020. Nationally, 61 percent of all drug reports in NFLIS were identified as involving methamphetamine (406,200 reports or 31 percent), cannabis/THC (167,669 reports or 13 percent), cocaine (165,162 reports or 12 percent), or heroin (72,315 reports or 5 percent). HHS Basis for Rec. at 44–45.

In 2021, there were 1,027,219 drug-specific cases submitted to and analyzed by State and local laboratories, a 2 percent increase from 2020. Although the total NFLIS-Drug number of drug reports increased in 2021 from 2020, the total number of cases and drugs reported continues to be noticeably lower than the numbers reported for the years before the COVID–19 pandemic. Nationally, in 2021, 45 percent of all drug cases contained one or more reports of methamphetamine, followed by cocaine (18 percent), cannabis/THC (17 percent), and heroin (8 percent). Nationally, the number of cannabis/THC reports as well as the number of cases in which cannabis/THC was identified decreased from 2015 through 2021, including a decrease from 188,735 to 167,669 from 2020 to 2021. HHS noted that this could mean there was a decrease in the number of cannabis/THC encounters, but it could also mean that there was a decrease in the number of exhibits submitted by law enforcement for analysis or a decrease in the number of exhibits processed (analyzed) by forensic laboratories. HHS Basis for Rec. at 45.

HHS Conclusion With Respect to Factor 5

In HHS's view, the most notable conclusion from its evaluation of epidemiological databases related to the medical outcomes from drug abuse is that, for all evaluated measures from 2015 to 2020, the rank order of comparators in terms of greatest adverse consequences typically placed alcohol (unscheduled), heroin (schedule I), and cocaine (schedule II) in the first or immediately subsequent position, with marijuana in a lower position. This pattern also held for PC data for serious medical outcomes, including death,

where marijuana was in the lowest ranking group. HHS determined that this demonstrated that there is consistency across databases, across substances, and over time, and that although abuse of marijuana produces clear evidence of harmful consequences, including SUD, the consequences are relatively less common and less harmful than some other comparator drugs. Additionally, HHS concluded, the number of law enforcement encounters with marijuana decreased from 2020 to 2021, at a time when law enforcement encounters were increasing for other scheduled drugs of abuse. However, as it noted with respect to Factor 1.A, HHS emphasized that there are limitations in comparing descriptive data on adverse outcomes across drugs, although descriptive analyses of epidemiologic data are an established practice in previous eight-factor analyses. HHS Basis for Rec. at 45.

In 2016, DEA found that abuse of marijuana is widespread and significant. 81 FR 53739. In addition, DEA found in 2016 that a significant proportion of all admissions for substance abuse treatment are for marijuana/hashish as the primary drug of abuse. *Id.* DEA notes that national data demonstrate that marijuana is one of the most widely used federally illicit substances in the United States, consistent with findings from the HHS Basis for Recommendation. According to the NSDUH, in 2022, among people aged 12 or older in the United States, an estimated 61.9 million people (22 percent) had used marijuana in the past year, and 42.3 million (15.0 percent) had used it in the past month. DEA notes that, according to one National Institutes of Health-supported study, the prevalence of daily marijuana use reached its highest level reported in 2021, at 11 percent of Americans aged 12 or older, a 3 percent increase from 2017 and a 5 percent increase from 2012.²⁷ It also notes that the average percentage of Δ9-THC in seized marijuana has increased over time.²⁸ Also, TEDS data showed that, in 2020, marijuana was the primary drug of admission in approximately 10 percent of all admissions to substance abuse treatment among patients aged 12 and older. HHS Basis for Rec. at 41, 46. DEA

²⁷ *Marijuana and hallucinogen use among young adults reached all time-high in 2021*, Nat'l Inst. on Drug Abuse (Aug. 22, 2022), <https://nida.nih.gov/news-events/news-releases/2022/08/marijuana-and-hallucinogen-use-among-young-adults-reached-all-time-high-in-2021>.

²⁸ *Cannabis Potency Data*, Nat'l Inst. on Drug Abuse (Nov. 23, 2022), <https://nida.nih.gov/research/research-data-measures-resources/cannabis-potency-data>.

also notes that TEDS data for 2021 reported that marijuana/hashish was the primary substance of abuse in 10.2 percent of all admissions to substance abuse treatment among patients aged 12 and older.²⁹ The 2021 TEDS data further reported that New York, California, Georgia, North Carolina, New Jersey, Texas, Minnesota, South Carolina, Florida, and Connecticut accounted for 55.9 percent of admissions to substance use treatments services where marijuana/hashish was listed as the primary substance.³⁰ DEA also believes that additional information regarding the scope, duration, and significance of marijuana abuse may be appropriate for consideration in assessing this factor.

6. What, if Any, Risk There Is to the Public Health

The sixth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the risk posed to the public health by marijuana. In analyzing this factor, HHS examined NSDUH data related to the demographics of U.S. individuals meeting criteria for marijuana use disorder, TEDS data related to the demographics of admission to treatment centers for marijuana use disorder, NEDS and NIS data on admissions to EDs and hospitals related to marijuana poisoning, ToxIC Core Registry data on intentional and unintentional exposure, and NPDS data describing the risks to youth of unintentional exposure to marijuana. HHS also assessed the risks to the public health through NSDUH data on driving under the influence of marijuana in adults and high school students. Finally, HHS reported data regarding the risk of serious AEs and death associated with nonmedical use/ use of uncertain intent of marijuana as reported to the FDA Adverse Event Reporting System, Center for Food Safety and Applied Nutrition Adverse Event Reporting System, National Vital Statistics System-Mortality ("NVSS-M"), DAWN, FDA's Sentinel Distributed Database System, and Centers for Medicare and Medicaid Services, and as reflected in the Drug-Involved Mortality data linking NVSS-M to death certificates. HHS Basis for Rec. at 46.

HHS Conclusion With Respect to Factor 6

HHS's detailed analysis of the risks posed by marijuana to the public health

²⁹ Substance Abuse & Mental Health Servs. Admin., *Treatment Episode Data Set (TEDS) 2021: Admissions to and Discharges from Substance Use Treatment Services Reported by Single State Agencies* 10 (2023), <https://www.samhsa.gov/data/sites/default/files/reports/rpt42794/2021-teds-annual-report.pdf> (Figure 3.A.9).

³⁰ *Id.* at 29 (Figure 6.B.4).

can be found at pages 46–57 of the HHS Basis for Recommendation. In summary, HHS found that the risks to the public health posed by marijuana are low compared to other drugs of abuse (e.g., heroin (schedule I), cocaine (schedule II)), based on its evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and, most importantly, for overdose deaths. The rank order of comparator drugs in terms of greatest adverse consequences typically places heroin, benzodiazepines, or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking, especially when comparing among individuals who reported using the respective drugs at least once in the prior year. For overdose deaths, marijuana is always ranked the lowest among comparator drugs. HHS interpreted these evaluations to demonstrate that there is consistent evidence across databases, across substances, and over time that, although the abuse of marijuana poses a risk to public health, the risk is relatively lower than that posed by most other comparator drugs. However, as HHS noted in its discussion of Factor 1, *see* HHS Basis for Rec. at 7–8, there are limitations in comparing descriptive data on adverse outcomes across drugs. HHS Basis for Rec. at 57.

In 2016, DEA found that, “[t]ogether with the health risks outlined in terms of pharmacological effects above, public health risks from acute use of marijuana include impaired psychomotor performance, impaired driving, and impaired performance on tests of learning and associative processes. Chronic use of marijuana poses a number of other risks to the public health including physical as well as psychological dependence.” 81 FR 53739–40. In addition to the data provided in the HHS Basis for Recommendation and the data considered by HHS and DEA in their prior eight-factor analyses, DEA anticipates that additional data on public safety risks, risks from acute and chronic marijuana use via oral and inhaled administration routes, and the impact of Δ9-THC potency may be appropriate for consideration.

As discussed in the HHS Basis for Recommendation, DEA notes that studies have examined the risk associated with marijuana use and driving. HHS Basis for Rec. at 50. The Rocky Mountain High Intensity Drug Trafficking Area reported in a publication that traffic deaths in Colorado in which drivers tested positive for marijuana more than doubled from 55 in 2013 to 131 in 2020,

although other evidence in the same report suggests that driving under the influence citations involving marijuana have grown at a rate similar to the rate for citations involving other drugs.³¹ DEA also identified some evidence suggesting that, among drivers who test positive for at least one drug in a traffic stop, a growing share test positive for cannabis.³²

7. Marijuana’s Psychic or Physiological Dependence Liability

The seventh factor that DOJ and HHS are required to consider under 21 U.S.C. 811(c) is the psychic or physiologic dependence liability of marijuana.

A. Psychic Dependence

The term “psychic or psychological dependence” has been used to refer to a state similar to addiction. For diagnosis purposes, the DSM–V has combined the diagnoses “abuse” and “drug dependence” (i.e., addiction), which the DSM’s Fourth Edition specified separately, into a single “substance use disorder,” which may occur in a broad range of severity, from mild to severe. HHS Basis for Rec. at 57.

The abuse potential of a drug can be assessed, in part, by evaluating the rewarding effects produced by that drug in humans and animals. As HHS described in its analysis of Factor 2, *see* HHS Basis for Rec. at 12–13, rodent behavioral studies show that Δ9-THC produces both self-administration and CPP. HHS determined that these results demonstrate that Δ9-THC has rewarding properties that are indicative of abuse potential. Further, as HHS described in its analysis of Factor 4, *see* HHS Basis for Rec. at 32–37, there is ample epidemiological evidence that marijuana is self-administered by humans, which may result from its ability to produce rewarding psychological effects, such as euphoria, *see* HHS Basis for Rec. at 15. HHS Basis for Rec. at 58.

In some individuals, extensive use of marijuana can lead to SUD. HHS noted that, in general, SUDs listed in the DSM–V are defined by an inability to cease drug use despite harmful consequences; Cannabis Use Disorder (“CUD”) shares this and other diagnostic criteria common to SUDs for other drugs of abuse. Estimates of CUD

in individuals who regularly use marijuana vary and range from about 10 to 20 percent. These estimates are similar to data from the United States National Comorbidity Study, which showed that 9 percent of lifetime cannabis users met the criteria for dependence outlined in the DSM’s revised Third Edition at some time in their life, compared to 32 percent of tobacco users, 23 percent of opiate users, and 15 percent of alcohol users. The National Epidemiologic Survey on Alcohol and Related Conditions also reported a nine percent lifetime cumulative probability of transitioning from marijuana use to dependence, with a higher risk of dependence in individuals with a history of psychiatric or other substance dependence comorbidity. In the United States, data from the 2020 NSDUH show that approximately 14 million individuals aged 12 or older who use marijuana or other cannabinoid preparations met criteria for CUD, representing 5.1 percent of all individuals aged 12 or older meeting the NSDUH survey inclusion criteria. HHS Basis for Rec. at 58.

Individuals who develop a SUD, including CUD, may seek treatment. From 2015 to 2020, TEDS documented approximately 10.8 million treatment episode admissions reported by individuals treated at publicly funded substance use treatment programs. Out of 1.4 million treatment admissions documented by TEDS in 2020, marijuana was reported as the primary substance of abuse in approximately 10 percent of admissions, making it the third most frequently reported primary substance of abuse, after alcohol (31.2 percent) and heroin (20.6 percent). A similar pattern was seen from 2015 to 2019. HHS Basis for Rec. at 58.

HHS concluded that the animal behavioral data show that Δ9-THC produces rewarding properties that underlie the abuse potential of marijuana. Epidemiological data demonstrate that some individuals who use marijuana for its rewarding properties go on to develop CUD, which shows that marijuana can produce psychological dependence. Among those individuals who seek admission for treatment for SUD associated with a drug of abuse, marijuana was the third most frequently reported primary substance of abuse. Thus, marijuana can produce psychic dependence in some individuals who use the drug. HHS Basis for Rec. at 58–59.

B. Physical Dependence

Physical dependence is a state of adaptation manifested by a drug-class

³¹ See 8 Rocky Mountain High Intensity Drug Trafficking Area, *The Legalization of Marijuana in Colorado: The Impact* 8, 13 (2021), https://www.rmhidta.org/files/ugd/4a67c3_b391ac360f974a8bbf868d2e3e25df3d.pdf. Note that the publication did not address the timing of marijuana use associated with fatal traffic accidents.

³² See Fernando A. Wilson et al., *Fatal Crashes from Drivers Testing Positive for Drugs, 1993–2010*, 129 Public Health Reports 342, 347–348 (2014).

specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, or administration of an antagonist. Although physical dependence is often associated with addiction, it can be produced by repeated administration of drugs both with and without abuse potential. HHS Basis for Rec. at 59.

As HHS discussed in its analysis of Factor 2, *see* HHS Basis for Rec. at 11, $\Delta 9$ -THC is a partial agonist at CB₁ receptors. When marijuana (or isolated $\Delta 9$ -THC) is administered chronically, there is a down-regulation of CB₁ receptors, which leads to behavioral tolerance. The underlying mechanism for marijuana withdrawal appears to be the uncoupling or desensitization of CB₁ receptors that precedes receptor down-regulation. Abrupt discontinuation of marijuana after prolonged administration produces withdrawal symptoms in rats and in humans that are typically opposite to those that occur with activation of the CB₁ receptor. Precipitated withdrawal can also be induced with administration of CB₁ antagonists following chronic administration, while administration of CB₁ agonists can attenuate some withdrawal symptoms associated with marijuana discontinuation. These data confirm the importance of the CB₁ receptor in marijuana physical dependence. HHS Basis for Rec. at 59.

HHS noted that research has not yet documented the occurrence of withdrawal symptoms in individuals who use marijuana only occasionally. However, in individuals who use marijuana heavily and chronically, drug discontinuation can lead to a withdrawal syndrome. Most marijuana withdrawal symptoms begin within 24 to 48 hours of drug discontinuation, peak within two to six days, and reduce over one to two weeks as $\Delta 9$ -THC levels decline. HHS Basis for Rec. at 59.

The most commonly reported withdrawal symptoms from clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness. Less commonly reported withdrawal symptoms include depressed mood, sweating, shakiness, physical discomfort, and chills. HHS described the symptoms of “cannabis withdrawal” listed in the DSM–V as being similar to those reported in the experimental studies, including nervousness or anxiety, irritability or aggression, insomnia or unpleasant dreams, depressed mood, decreased appetite or weight loss, restlessness, abdominal pain, shakiness or tremors, sweating,

fever, chills, and headache. HHS Basis for Rec. at 59–60.

HHS reported that up to 40 to 50 percent of individuals who use marijuana on a regular basis may experience physical dependence. A meta-analysis of 23,518 individuals who frequently used marijuana showed that 47 percent of subjects reported symptoms of marijuana withdrawal. The prevalence of physical dependence was 54 percent in outpatient samples, 17 percent in community samples, and 87 percent among inpatients in drug abuse treatment centers. This is consistent with data showing that 90 percent of individuals who were diagnosed with CUD also reported physical dependence. Further, individuals diagnosed with CUD experience more severe and longer lasting withdrawal symptoms when discontinuing marijuana than individuals who do not have a diagnosis of CUD. This may be because individuals with CUD have greater exposure to marijuana. HHS Basis for Rec. at 60.

Symptoms associated with marijuana withdrawal appear to be relatively mild compared to those associated with alcohol withdrawal, which can include agitation, paranoia, seizures, and even death. Multiple studies comparing the withdrawal symptoms associated with tobacco (not scheduled in the CSA) and marijuana demonstrate that the magnitude and time course of the two withdrawal syndromes are similar. Animal studies have shown that after short-term administration of equianalgesic doses of heroin and $\Delta 9$ -THC to monkeys, withdrawal signs were observed after heroin administration but not after $\Delta 9$ -THC administration, further demonstrating that withdrawal from marijuana is associated with less severe symptoms than withdrawal from other drug classes. HHS Basis for Rec. at 60.

HHS Conclusion With Respect to Factor 7

In conclusion, HHS found experimental and clinical evidence that chronic, but not acute, use of marijuana can produce both psychic and physical dependence in humans. Epidemiological data, discussed in greater detail in the sections describing Factors 4 and 5 in sections VI.4 and VI.5 of this preamble, provide additional evidence of psychic dependence. The symptoms associated with both kinds of dependence are relatively mild for most individuals, although their severity may be greater with increased exposure to marijuana. HHS Basis for Rec. at 61.

In 2016, DEA found that “[l]ong-term, heavy use of marijuana can lead to physical dependence and withdrawal

following discontinuation, as well as psychic or psychological dependence.” 81 FR 53740. DEA notes that some physicians have argued that CUD is underdiagnosed and undertreated in the medical setting,³³ and that other medical professionals have noted that CUD needs to be better understood and characterized to better inform users and treatment professionals.³⁴ DEA anticipates that additional psychic or physiological dependence liability may be appropriate for consideration.

8. Whether Marijuana Is an Immediate Precursor of a Substance Already Controlled Under the CSA

The eighth factor that DOJ and HHS are required to consider under 21 U.S.C. 811(c) is whether marijuana is an immediate precursor of a substance already controlled under the CSA. HHS concluded that marijuana is not an immediate precursor of another controlled substance. HHS Basis for Rec. at 61. This finding is consistent with DEA’s finding in 2016. 81 FR 53740. DEA welcomes additional information on this factor.

VII. Determination of Appropriate Schedule for Marijuana

After conducting the eight-factor analysis in 2023, HHS has recommended three findings regarding the appropriate schedule in which to place marijuana. The three findings relate to: (1) a substance’s abuse potential; (2) whether the substance has a CAMU; and (3) the safety or dependence potential of the substance. 21 U.S.C. 812(b); HHS Basis for Rec. at 62–65.

1. Potential for Abuse

In 2016, HHS found that many factors indicated marijuana’s high abuse potential, “including the large number of individuals regularly using marijuana, marijuana’s widespread use, and the vast amount of marijuana available for illicit use.” 81 FR 53688 at 53706. As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS has recommended a finding that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II.

³³ See, e.g., Theresa A. Matson et al., *Association Between Cannabis Use Disorder Symptom Severity and Probability of Clinically-Documented Diagnosis and Treatment in a Primary Care Sample*, 251 Drug & Alcohol Dependence, no. 110946, 2023.

³⁴ See, e.g., Gwen T. Lapham et al., *Prevalence of Cannabis Use Disorder and Reasons for Use Among Adults in a U.S. State Where Recreational Cannabis Use is Legal*, 6 JAMA Open no. e2328934, 2023, at 7.

Marijuana contains $\Delta 9$ -THC (also known as dronabinol when specifically referring to (-)-*trans*- $\Delta 9$ -THC stereoisomer), the substance responsible for the abuse potential of marijuana. $\Delta 9$ -THC has agonist properties at CB₁ cannabinoid receptors and produces rewarding responses in animals, as evidenced by its ability to produce self-administration and CPP. When marijuana is administered to humans under experimental conditions, it produces a wide range of positive subjective responses in addition to certain negative subjective responses. Common responses to marijuana when it is used by individuals for nonmedical purposes include euphoria and other positive subjective responses, as well as perceptual changes, sedative responses, anxiety responses, psychiatric, social, and cognitive changes, and physiological changes. HHS Basis for Rec. at 62.

HHS noted that epidemiological data from NSDUH show that marijuana is the most frequently used federally illicit drug in the United States on a past-year and past-month basis among the illicit comparator drugs considered. Although 50 percent of respondents in NSDUH reported using marijuana nonmedically fewer than 5 days per month, another 30 percent reported using it nonmedically for 20 days or more per month. HHS Basis for Rec. at 62.

Despite the high prevalence of nonmedical use of marijuana, HHS observed that an overall evaluation of epidemiological indicators suggests that it does not produce serious outcomes compared to drugs in schedules I or II. HHS found this especially notable given the availability of marijuana and marijuana-derived products that contain extremely high levels of $\Delta 9$ -THC. Due to such availability, the epidemiological data described in HHS's evaluation inherently include the outcomes from individuals who use marijuana and marijuana-derived products that have doses of $\Delta 9$ -THC that range from low to very high, and yet the data demonstrate that these products overall are producing fewer negative outcomes than drugs in schedules I or II. HHS Basis for Rec. at 62.

HHS compared the rank ordering of selected drugs that are abused for various epidemiological measures and observed that marijuana was among the drugs at the very lowest ranking for a number of measures, including PC abuse cases, likelihood that any use would lead to a PC call, accidental or unintentional poisoning, utilization-adjusted rates of unintentional exposure, utilization-adjusted and population-adjusted rates for ED visits

and hospitalizations, likelihood of being diagnosed with a serious SUD, deaths reported to PCs, and overdose deaths when used with other drugs or as a single substance (as total numbers and when utilization-adjusted). In contrast, comparators such as heroin (schedule I), oxycodone (schedule II), and cocaine (schedule II) typically were in the highest rank ordering on these measures. HHS Basis for Rec. at 62.

For the various epidemiological measures evaluated above, HHS noted that marijuana was also compared to controlled substances in schedule III (ketamine) and schedule IV (benzodiazepines, zolpidem, and tramadol), as well as to other schedule II substances (fentanyl and hydrocodone). The analyses were conducted in this manner to provide a comprehensive assessment of the relative abuse potential of marijuana. However, the rank order of these substances regarding harms does not consistently align with the relative scheduling placement of these drugs in the CSA due to the pharmacological differences between various classes of drugs. HHS Basis for Rec. at 63.

There are a number of confounding factors that likely influence the adverse outcomes measured in various epidemiological databases and account for the rank ordering of the drugs evaluated on these measures. For example, a different population abuses each substance, and each substance has a different prevalence of abuse and a different profile of severe adverse outcomes in a setting of nonmedical use and abuse. Thus, it is challenging to reconcile the ranking of relative harms associated with the comparators used in this evaluation when the rankings differ across various epidemiological databases and when these rankings often do not align with the scheduling placement of these comparators under the CSA. HHS Basis for Rec. at 63.

To address these challenges, HHS evaluated the totality of the available data and has concluded that it supports the placement of marijuana in schedule III. Overall, these data demonstrate that, although marijuana is associated with a high prevalence of abuse, the profile of and propensity for serious outcomes related to that abuse lead to a conclusion that marijuana is most appropriately controlled in schedule III under the CSA. HHS Basis for Rec. at 63.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight at this stage of the scheduling process. *See* OLC Op. at *22

n.6 ("HHS's recommendations with respect to 'scientific and medical matters' are binding for all eight factors listed in section 811(c)."). The Attorney General concurs with HHS's recommendation, for purposes of initiation of these rulemaking proceedings, that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II.

2. Currently Accepted Medical Use in Treatment in the United States

In 2016, HHS recommended a finding that marijuana had no CAMU due in part to a lack of adequate safety studies or evidence that qualified experts accepted marijuana for use in treating a specific, recognized disorder. 81 FR 53688 at 53707. As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS recommends a finding that marijuana has a CAMU.

In making that recommendation, HHS analyzed whether there is (1) widespread current experience with medical use of the substance in the United States by licensed health care practitioners operating in accordance with implemented State-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine; and (2) some credible scientific support for a least one of those medical uses. Applying this test, HHS recommended a finding that marijuana has a currently accepted medical use in the United States, specifically for the treatment of anorexia related to a medical condition, nausea and vomiting (*e.g.*, chemotherapy-induced), and pain. According to HHS, its evaluation also supported a finding that there is accepted safety for the use of marijuana under medical supervision for the treatment of anorexia related to a medical condition, nausea and vomiting (*e.g.*, chemotherapy-induced), and pain. HHS Basis for Rec. at 63–64.

In the past, DEA has concluded that a substance has a CAMU under the CSA only if one of two tests is satisfied. First, DEA has determined that a substance has a CAMU if the substance has been approved by FDA for marketing under the FDCA, either through the NDA process or by meeting the criteria to be recognized as a "Generally Recognized As Safe and Effective" ("GRASE") drug. 57 FR 10499, 10503 (March 26, 1992). Second, DEA has determined a substance has a CAMU if the substance satisfies a five-part test established by DEA in 1992 that was based on the "core FDCA standards for acceptance of drugs for medical use":

1. There must be adequate safety studies;
2. The drug's chemistry must be known and reproducible;
3. There must be adequate and well-controlled studies proving efficacy;
4. The drug must be accepted by qualified experts; and
5. The scientific evidence must be widely available.

57 FR 10499, 10503–06 (1992); *see also All. for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994).

In its most recent evaluation, HHS informed DEA of its view that DEA's previous approach to determining whether a drug has a CAMU does not adequately account for certain indicia of medical use that, where present, are relevant to determining whether a substance has a CAMU for purposes of scheduling under the CSA. Specifically, HHS observed that DEA's tests left no room for an evaluation of (1) whether there is widespread medical use of a drug under the supervision of licensed health care practitioners under State-authorized programs and, (2) if so, whether there is credible scientific evidence supporting such medical use. HHS therefore developed an alternative test composed of those two inquiries as a third, independently sufficient approach for determining whether a substance has a CAMU under the CSA. HHS applied this two-part test to marijuana and recommended a finding that marijuana has a CAMU under the CSA. HHS Basis for Rec. at 24–28.

Upon receiving HHS's recommendation, the Attorney General requested that OLC advise on whether HHS's test, if satisfied, established a CAMU “even if the drug has not been approved by FDA and even if the drug does not satisfy DEA's five-part test.” OLC Op. at *3. OLC determined that DEA's current approach to determining whether a drug has a CAMU is impermissibly narrow, because it “ignor[es] widespread clinical experience with a drug that is sanctioned by state medical licensing regulators.” *Id.* at *13–14; *see also id.* at *12. OLC further opined that satisfying HHS's two-part inquiry is sufficient to establish that a drug has a CAMU. *Id.* at *4, *16–20. And OLC concluded that, while HHS's CAMU recommendation is not binding on DEA, the medical and scientific determinations that underlie its recommendation are binding until the initiation of formal rulemaking proceedings, and that DEA must accord those determinations “significant deference” throughout the rulemaking process. *Id.* at *4, *20–26.

Under Part 1 of the HHS CAMU test, the Office of the Assistant Secretary for

Health (“OASH”) considered whether there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented State-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these State jurisdictions. Part 2 of the CAMU test evaluated whether there exists some credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied. The evaluation in Part 2, undertaken by FDA, was not meant to be, nor is it, a determination of safety and efficacy under the Federal Food, Drug, and Cosmetic Act's drug approval standard for new human or animal drugs. Rather, HHS's two-part test is designed to evaluate whether a substance, in this case marijuana, has a CAMU for purposes of drug scheduling recommendations and placement in a drug schedule consistent with criteria set forth in 21 U.S.C. 812(b). HHS Basis for Rec. at 24.

In the evaluation and assessment under Part 1 of the CAMU test, OASH found that more than 30,000 HCPs are authorized to recommend the use of marijuana for more than six million registered patients, constituting widespread clinical experience associated with various medical conditions recognized by a substantial number of jurisdictions across the United States. For several jurisdictions, these programs have been in place for several years, and include features that actively monitor medical use and product quality characteristics of marijuana dispensed. HHS Basis for Rec. at 24.

Based on OASH's findings in Part 1 of the CAMU test, the Assistant Secretary for Health concluded that an FDA assessment under Part 2 of the CAMU test was warranted to determine if credible scientific support exists for the use of marijuana to treat at least one of the medical conditions identified by OASH under Part 1. HHS Basis for Rec. at 24.

At this stage of initiating a rulemaking, the Attorney General agrees with OASH that there is widespread clinical experience with marijuana for at least one medical condition.

FDA conducted Part 2 of the CAMU test for seven indications, based in part on OASH's findings under Part 1 of the CAMU test³⁵ and in part on FDA's own

³⁵ In Part 1 of the CAMU test, OASH identified at least 15 medical conditions for which there is widespread current experience with medical use of marijuana in the United States by licensed HCPs

analysis of the landscape in which marijuana is currently used medically, including information from State-authorized programs on how and to what extent marijuana is being utilized for medical purposes. The seven indications are: (1) anorexia;³⁶ (2) anxiety;³⁷ (3) epilepsy; (4) inflammatory bowel disease (“IBD”); (5) nausea and vomiting; (6) pain; and (7) post-traumatic stress disorder (“PTSD”). FDA's evaluation under Part 2 of the CAMU test was based on systematic reviews of studies investigating the safety and effectiveness of marijuana, relevant professional societies' position statements, data from State medical marijuana programs and United States national surveys, and the labeling of FDA-approved products relevant to the analysis. HHS Basis for Rec. at 25.

In evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors in favor of a positive finding included whether: (1) favorable clinical studies of the medical use of marijuana, although not necessarily adequate and well-controlled clinical studies that would support approval of an NDA, have been published in peer-reviewed journals or (2) qualified expert organizations (e.g., academic groups, professional societies, or government agencies) have opined in favor of the medical use or provided guidance to HCPs on the medical use. Factors that weigh against a finding that Part 2 of the CAMU test is met included whether: (1) data or information indicate that medical use of the substance is associated with unacceptably high

operating in accordance with implemented State-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine. These conditions include amyotrophic lateral sclerosis (commonly known as ALS), autism, cachexia, cancer, chronic pain, Crohn's disease, epilepsy or condition causing seizures, glaucoma, HIV/AIDS, multiple sclerosis, Parkinson's disease, persistent/severe muscle spasm, persistent/severe nausea, PTSD, and spasticity. FDA conducted Part 2 of the analysis for the medical conditions identified by OASH that were likely to have the most robust evidence available for review; because the analysis concluded that the Part 2 test has been met for at least one of the conditions identified in Part 1, there was no need to analyze all of them. HHS Basis for Rec. at 25 n.9.

³⁶ The anorexia indication reflects anorexia due to a medical condition (e.g., HIV/AIDS) and does not represent anorexia nervosa. HHS Basis for Rec. at 25 n.10.

³⁷ While anxiety was not one of the specific medical conditions identified by OASH, it is included herein because anxiety was identified by the FDA during the Part 2 review of State-level usage data. FDA considered the medical use of marijuana for the treatment of anxiety of importance to evaluate given the reported prevalence of marijuana use for the treatment of anxiety regardless of the legal status of such use in a given jurisdiction. HHS Basis for Rec. at 25 n.11.

safety risks for the likely patient population, *e.g.*, due to toxicity concerns; (2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; or (3) qualified expert organizations (*e.g.*, academic or professional societies, government agencies) recommend against the medical use of marijuana based on the available data at the time of their position statement. HHS Basis for Rec. at 25.

FDA's review of the available information identified mixed findings of effectiveness across indications, ranging from data showing inconclusive findings to considerable evidence in favor of effectiveness, depending on the source. The largest evidence base for effectiveness exists for marijuana use within the pain indication (in particular, neuropathic pain). Numerous systematic reviews concluded that there exists some level of evidence supporting the use of marijuana for chronic pain. The 2017 NASEM report concluded there was "substantial evidence"³⁸ supporting the use of cannabis products relevant to this review for pain, as have other reviews. The AHRQ living systematic review has concluded that there is some support for the use of marijuana-related products in the treatment of chronic pain, but overall concluded these effects were small and the increased risk of dizziness, nausea, and sedation may limit the benefit. A systematic review of scientific and medical literature was conducted in 2023 by the University of Florida ("UF") under contract with FDA. UF epidemiologists identified some data supporting effectiveness of marijuana, including some within their own meta-analysis; however, they ultimately concluded the results are inconclusive or mixed. FDA also conducted a separate analysis of published scientific reviews, several of which drew conclusions similar to those of UF. HHS Basis for Rec. at 25–26.

UF evaluated other therapeutic conditions mentioned above, *i.e.*, anorexia, anxiety, epilepsy, IBD, nausea, and PTSD, employing a similar systematic review of scientific and medical literature. UF found that there is low- to moderate-quality evidence supporting the use of marijuana as medical treatment for outcomes in anorexia, nausea and vomiting, and PTSD. FDA's review of systematic reviews showed mixed results for these

indications. In particular, FDA found that the potential for psychiatric adverse events associated with treating PTSD with marijuana may be more substantial than any limited benefit in observational studies. Although UF did not conclude that there was evidence in support of the effectiveness of marijuana in IBD, both their review and other systematic reviews found some benefit with respect to subjective symptoms in this condition. With regard to epilepsy and anxiety, both UF's review and FDA's review of other systematic reviews did not find support for marijuana providing benefit in the treatment of these conditions. Where positive results on effectiveness outcome measures were found, the effects and the quality of evidence were generally in the low-to-moderate range. UF did not find high quality evidence supporting worsening of outcomes in any indication. HHS Basis for Rec. at 26.

FDA concluded that none of the evidence from the systematic reviews included in the CAMU test Part 2 analysis identified any safety concerns that would preclude the use of marijuana in the indications for which there exists some credible scientific support for its therapeutic benefit. FDA assessed the clinical safety data identified in the literature from controlled trials as generally consistent between sources but limited in the rigor of safety reporting. FDA also explained that the vast majority of the observational studies evaluated in the context of medical use were excluded from the final synthesis of evidence due to concerns regarding their quality (*e.g.*, only one observational study for the anxiety indication and one for the PTSD indication were included). According to FDA, data on safety from both clinical trials and observational studies were generally scarce, but the literature shows that marijuana has more AEs when compared to a placebo or active control group, however, typically in the mild to moderate severity range. HHS Basis for Rec. at 26.

FDA also reviewed results from State reporting data from 37 States with medical marijuana programs and surveys of patients using marijuana in Maryland and Minnesota, which had data available for review. Surveys of patients using marijuana in these two States found most patients did not report any side effects and those that did report side effects mostly described them as mild. Neither State's databases included patients who chose to stop using marijuana, which FDA noted might result in an overestimation of positive experiences. HHS Basis for Rec. at 27.

As of August 2023, FDA reported that the real-world data sources available to FDA, in general, lack the necessary elements to identify the exposure (*i.e.*, to marijuana), to distinguish the reason for use (medical vs. recreational) and, if applicable, the condition that prompted its medical use, and to permit sound inferential analyses. Therefore, they were not included in HHS's review. HHS Basis for Rec. at 27.

According to FDA, data from United States national surveys, in general, lacked details on patient characteristics and factors that prompted the use of marijuana for medical purposes, and data collection for these surveys was impacted by the COVID-19 pandemic. FDA observed that, despite these limitations, the data suggested that medical use of marijuana increases as age increases. Only data from one survey provided information on the intended indication for use, suggesting that individuals often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms, but only approximately half of them reportedly had ever asked a health care professional for a recommendation to use medical marijuana. HHS Basis for Rec. at 27.

Additionally, although the safety data obtained from use in a medical context are considered to be the most relevant for the CAMU analysis, FDA evaluated the safety of marijuana in the nonmedical setting to inform the potential for more severe outcomes. Specifically, FDA evaluated safety outcomes related to marijuana use in the setting of nonmedical use, use of uncertain intent, and unintentional exposure through a variety of epidemiological data sources and in relation to several comparator substances controlled under the CSA, including drugs in schedule I: heroin (an illicit opioid drug); schedule II: hydrocodone and oxycodone (approved opioid prescription drug products), cocaine and fentanyl (largely illicitly produced drugs in the nonmedical use setting, although there are approved prescription drugs); schedule III: ketamine (an approved prescription drug); and schedule IV: zolpidem, benzodiazepines, and tramadol (approved prescription drugs). According to FDA, the comparative data demonstrate that, even in the context of nonmedical use, marijuana has a less concerning overall safety profile relative to the comparators for a number of important outcomes (*e.g.*, single substance use overdose death,

³⁸ The term "substantial evidence" refers to language used within the 2017 NASEM report and is not meant to represent "substantial evidence" as defined in 21 U.S.C. 355(d). HHS Basis for Rec. at 26 n.12.

hospitalizations). However, FDA observed that in young children, population-adjusted rates of ED visits and hospitalizations involving marijuana poisoning were higher than heroin, cocaine, and benzodiazepines for the periods studied. Of note, some of the comparator substances are approved for use in conditions similar to the indications for which marijuana was evaluated in the CAMU analysis (e.g., opioids for pain, benzodiazepines for anxiety-related conditions). HHS Basis for Rec. at 27.

FDA also considered position statements from professional organizations relevant to the indications discussed. The vast majority of professional organizations did not recommend the use of marijuana in their respective specialties; however, none specifically recommended against it, with the exception of the American Psychiatric Association, which stated that marijuana is known to worsen certain psychiatric conditions. HHS Basis for Rec. at 27–28.

On balance, FDA found the available data indicated that there is some credible scientific support for the use of marijuana in the treatment of chronic pain, anorexia related to a medical condition, and nausea and vomiting, with varying degrees of support and consistency of findings. Additionally, no safety concerns were identified in FDA's review that would indicate that medical use of marijuana poses unacceptably high safety risks for the indications where there is some credible scientific evidence supporting its therapeutic use. HHS Basis for Rec. at 28.

Based on the totality of the available data, FDA concluded that there exists some credible scientific support for the medical use of marijuana in at least one of the indications for which there is widespread current experience in the United States, as identified by OASH under Part 1 of the CAMU test. The indications evaluated were anorexia related to a medical condition, anxiety, epilepsy, IBD, nausea and vomiting (e.g., chemotherapy-induced), pain, and PTSD. FDA clarified that the analysis and conclusions on the available data are not meant to imply that safety and effectiveness have been established for marijuana that would support FDA approval of a marijuana drug product for a particular indication. However, FDA determined that the available data do provide some level of support for the way marijuana is being recommended by health care practitioners in clinical practice. Thus, based on the widespread HCP experience and the extent of medical use evaluated by OASH under

the Part 1 test, and FDA's evaluation of available credible scientific support described herein for at least some therapeutic uses identified in the Part 1 test, HHS recommended a finding that, for purposes of the drug scheduling criteria in 21 U.S.C. 812(b), marijuana has a CAMU for: anorexia related to a medical condition; nausea and vomiting (e.g., chemotherapy-induced); and pain. HHS Basis for Rec. at 28.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight until the initiation of the formal rulemaking process. *See* OLC Op. at *24. Applying HHS's two-part test, and in light of OLC's legal opinion that the HHS's test is sufficient under the CSA, the Attorney General concurs with HHS's conclusion, for purposes of the initiation of these rulemaking proceedings, that there is a CAMU for marijuana.

3. Level of Physical or Psychological Dependence

As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS has recommended a finding that abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence. HHS Basis for Rec. at 65.

According to HHS, clinical studies have demonstrated that marijuana produces physical and psychological dependence. Regarding physical dependence, as evidenced by its associated withdrawal symptomatology upon abrupt discontinuation of use, the most commonly reported marijuana withdrawal symptoms in clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness. Marijuana withdrawal symptoms typically peak within two to six days and decline over one to two weeks as Δ 9-THC is eliminated. Similarly, the drug labels for the FDA-approved drug products Marinol and Syndros state that, following chronic administration of dronabinol, drug discontinuation leads to irritability, insomnia, and restlessness at 12 hours, and by 24 hours the withdrawal symptoms can include hot flashes, sweating, rhinorrhea, diarrhea, and anorexia. HHS Basis for Rec. at 64.

HHS observes that marijuana withdrawal syndrome has been reported in individuals with heavy, chronic marijuana use, but its occurrence in occasional users of marijuana has not been established. The marijuana

withdrawal syndrome appears to be relatively mild compared to the withdrawal syndrome associated with alcohol, which can include more serious symptoms such as agitation, paranoia, seizures and even death. Multiple studies comparing the withdrawal symptoms associated with marijuana and tobacco demonstrate that the magnitude and time course of the two withdrawal syndromes are similar. HHS Basis for Rec. at 64.

HHS also notes that the ability of marijuana to produce psychic dependence is shown through its ability to produce rewarding effects that underlie its nonmedical use and epidemiological outcomes related to abuse, as detailed in the first finding on abuse potential. HHS Basis for Rec. at 64–65.

Based on the evidence, HHS determined that the abuse of marijuana may lead to moderate or low physical dependence, depending on frequency and degree of marijuana exposure. HHS further concluded that marijuana can produce psychic dependence in some individuals, but that the likelihood of serious outcomes is low, suggesting that high psychological dependence does not occur in most individuals who use marijuana. HHS Basis for Rec. at 65.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight at this stage of the scheduling process. *See* OLC Op. at *22 n.6. For purposes of the initiation of these rulemaking proceedings, the Attorney General concurs with HHS's conclusion that the abuse of marijuana may lead to moderate or low physical dependence, depending on frequency and degree of marijuana exposure.

Determination To Propose Rescheduling Marijuana to Schedule III

HHS has recommended a finding that marijuana has a CAMU. HHS Basis for Rec. at 63–64. After considering the foregoing facts and data and the recommendation of HHS, and after according binding weight to HHS's scientific and medical determinations, the Attorney General concludes that there is, at present, substantial evidence that marijuana does not warrant control under schedule I of the CSA. Accordingly, the Attorney General is issuing this notice of proposed rulemaking to initiate rulemaking proceedings to reschedule marijuana. 21 U.S.C. 811(b).

HHS has recommended that marijuana be transferred from schedule I to schedule III rather than from schedule I to schedule II based on its

evaluation that the drug has a relatively lower level of abuse compared to drugs currently scheduled in schedules I and II and its evaluation that marijuana may lead to moderate or low physical dependence and has a low likelihood of psychic dependence. Consistent with HHS's analysis, the Attorney General has determined at this initial stage that marijuana does not appear to meet the elements of a schedule II drug, which include a high potential for abuse and a likelihood of severe physiological or physical dependence from such abuse. 21 U.S.C. 812(b)(3). Rather, marijuana's profile as a drug with a lower degree of abuse potential than schedule I (e.g., heroin) and schedule II (e.g., fentanyl, cocaine) drugs and a moderate to low level of physical dependence militates in favor of rescheduling it in schedule III. Accordingly, in this notice of proposed rulemaking, the Attorney General is proposing to reschedule marijuana in schedule III and solicits comments on these preliminary findings.

Types of Marijuana To Be Rescheduled

This rescheduling of marijuana would apply to marijuana as listed in 21 CFR 1308.11(d)(23). The rescheduling also would apply to marijuana extracts as defined in 21 CFR 1308.11(d)(58) because they meet the statutory definition of marijuana and, prior to 2017, were included in 21 CFR 1308.11(d)(23). See *Establishment of a New Drug Code for Marihuana Extract*, 81 FR 90194 (Dec. 14, 2016). In addition, this proposal would apply to Δ9-THC derived from the marijuana plant (other than the mature stalks and seeds) that falls outside the definition of hemp, because it meets the statutory definition of marijuana.

This proposal would not apply to synthetically derived THC, which is outside the CSA's definition of marijuana. Those tetrahydrocannabinols that can be derived only through a process of artificial synthesis (e.g., delta-10-tetrahydrocannabinol) are excluded. HHS provided a recommendation only relating to "marijuana" as defined in the CSA. That definition is limited to the plant (other than the mature stalks and seeds) and derivatives of the plant. Therefore, synthetic THC will remain in schedule I. This rulemaking would not affect the status of hemp (as defined in 7 U.S.C. 1639o), because hemp is excluded from the definition of marijuana. This rulemaking is not proposing to reschedule any drug product containing marijuana or THC that previously has been rescheduled out of schedule I (e.g., Marinol and Syndros). Nor does it impact the status

of any previously scheduled synthetic cannabinoids.

VIII. International Treaty Obligations

In proposing an appropriate schedule for marijuana, the Attorney General must also consider compliance with the treaty obligations of the United States. As the CSA recognizes, the United States is a party to the Single Convention. 21 U.S.C. 801(7). Parties to the Single Convention are obligated to maintain various control provisions related to the drugs that are covered by the treaty. See, e.g., Single Convention arts. 2, 4. Congress enacted many of the CSA's provisions for the specific purpose of ensuring U.S. compliance with the treaty. See OLC Op. at *27. Among these is a scheduling provision, 21 U.S.C. 811(d)(1). Section 811(d)(1) provides that, where a drug is subject to control under the Single Convention, the Attorney General must "issue an order controlling such drug under the schedule he deems most appropriate to carry out such [treaty] obligations, without regard to the findings required by [21 U.S.C. 811(a) or 812(b)] and without regard to the procedures prescribed by [21 U.S.C. 811(a) and (b)]." ³⁹

Marijuana is a drug covered in the Single Convention under the term "cannabis." ⁴⁰ OLC initially advised in 1972 that controls under Article 21 of the Single Convention would not be satisfied if marijuana were listed in schedule III, IV, or V of the CSA. Memorandum for John E. Ingersoll,

³⁹ As noted above, OLC and the D.C. Circuit do not understand the "without regard" clause in section 811(d)(1) as prohibiting the Attorney General from following the normal scheduling practices when international obligations are involved. Instead, they have interpreted it as requiring the Attorney General to identify which schedules would satisfy the international obligations of the United States with respect to a particular drug and, if more than one schedule would do so, to select among schedules using the procedures set forth in sections 811(a), 811(b), and 812(b). See OLC Op. at *29 n.8; *NORML II*, 559 F.2d at 747.

⁴⁰ Under the Single Convention, "[c]annabis plant" means any plant of the genus *Cannabis*. Single Convention art. 1(1)(c). The Single Convention defines "cannabis" to mean "the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted, by whatever name they may be designated." *Id.* art. 1(1)(b). This definition of "cannabis" under the Single Convention is slightly less inclusive in certain respects than the CSA definition of "marijuana," which includes all parts of the cannabis plant except for the mature stalks, sterilized seeds, oil from the seeds, and certain derivatives thereof. See 21 U.S.C. 802(16). Cannabis and cannabis resin are included in the list of drugs in Schedule I of the Single Convention, and cannabis is subject to the same controls as Schedule I drugs as well as additional controls. See Single Convention art. 2(6); *id.* art. 28.

Director, Bureau of Narcotics and Dangerous Drugs, from Mary C. Lawton, Deputy Assistant Attorney General, Office of Legal Counsel, *Re: Petition to Decontrol Marihuana; Interpretation of Section 201 of the Controlled Substances Act of 1970 at 12–13* (Aug. 21, 1972). However, OLC has reexamined the conclusion of its 1972 memorandum, taking into account statutory amendments since 1972 and a possibility it did not consider in 1972: placing marijuana into schedule III while issuing regulations that would enable the United States to comply with its international obligations. OLC Op. at *4, 26–35. OLC has concluded that both the Single Convention and the CSA allow the Attorney General to satisfy the treaty obligations of the United States with respect to marijuana by supplementing scheduling decisions with additional controls under the CSA. *Id.*

If marijuana were listed in schedule III, most of the Single Convention's obligations would continue to be met by CSA statutory authorities and associated regulations. See OLC Op. at *33–34. One potential gap concerns the quota on manufacturing cannabis required by Article 21 of the Convention, but that gap can be filled using the CSA's regulatory authorities. See *id.* at *34; see also, e.g., 21 U.S.C. 821 (authorizing the Attorney General to impose restrictions "related to the . . . control of the manufacture" of a drug); *id.* 871(b) (authorizing the Attorney General to issue regulations "necessary and appropriate for the efficient execution of his functions under this subchapter"); *id.* 822(b) (allowing the Attorney General to regulate "the extent" of manufacture of a drug through registration); *id.* 823(e) (requiring the Attorney General to register an applicant to manufacture a schedule III drug "unless he determines that the issuance of such registration is inconsistent with the public interest").

In addition, if marijuana is transferred into schedule III, DEA will continue to have authority to maintain its existing regulatory scheme, located at 21 CFR part 1318, governing the registration of manufacturers seeking to plant, grow, cultivate, or harvest marijuana, as required to comply with Articles 23 and 28 of the Single Convention. Authority for those regulations currently flows from 21 U.S.C. 823(a), which is applicable to drugs in schedules I and II. OLC has concluded, however, that 21 U.S.C. 823(e), which is applicable to drugs in schedules III, IV, and V, provides an alternative source of authority for complying with Articles 23 and 28 of the Single Convention. See

OLC Op. at *34 n.9. The CSA also recognizes that the United States is also a party to the Convention on Psychotropic Substances, Feb. 21, 1971, 32 U.S.T. 543, 1019 U.N.T.S. 175 (“Convention on Psychotropic Substances”). See also 21 U.S.C. 801a(2). As with the Single Convention, parties to the Convention on Psychotropic Substances are obligated to take various control measures related to the drugs that are covered by the treaty. *Id.* Congress implemented the additional authority necessary to comply with the Convention on Psychotropic Substances through various amendments to the CSA. *Id.* 801a(2)–(3).

Δ9-THC is a substance covered by schedule II of the Convention on Psychotropic Substances. In this rule, DOJ proposes to reschedule Δ9-THC that falls within the CSA’s definition of marijuana into CSA schedule III. As is the case for marijuana under the Single Convention, the controls available under CSA schedule III are sufficient to comply with the requirements of the Convention on Psychotropic Substances with respect to Δ9-THC, although additional regulatory action may be necessary to implement certain Convention requirements, such as the export and import authorizations required by Article 12. See, e.g., *Schedules of Controlled Substances: Rescheduling of the Food and Drug Administration Approved Product Containing Synthetic Dronabinol [(–)-D⁹-(trans)-Tetrahydrocannabinol] in Sesame Oil and Encapsulated in Soft Gelatin Capsules From Schedule II to Schedule III*, 64 FR 35928, 35928 (July 2, 1999). Compare, e.g., Convention on Psychotropic Substances art. 12(1) (requiring export and import authorizations for substances in Convention Schedule II), with 21 U.S.C. 952(b)(2) (authorizing import permits for CSA schedule III substances), and *id.* 953(e)(2) (authorizing export permits for CSA schedule III substances).

Accordingly, concurrent with this rulemaking, DEA will consider the marijuana-specific controls that would be necessary to meet U.S. obligations under the Single Convention and the Convention on Psychotropic Substances in the event that marijuana is rescheduled to schedule III, and, to the extent they are needed if marijuana is rescheduled, will seek to finalize any such regulations as soon as possible.

IX. Requirements for Handling Marijuana and Other Applicable Controls

If marijuana is transferred to schedule III, the regulatory controls applicable to

schedule III controlled substances would apply, as appropriate, along with existing marijuana-specific requirements and any additional controls that might be implemented, including those that might be implemented to meet U.S. treaty obligations. The manufacture, distribution, dispensing, and possession of marijuana would also remain subject to applicable criminal prohibitions under the CSA. 21 U.S.C. 841–844.

In addition, marijuana would remain subject to applicable provisions of the FDCA. For example, under the FDCA, a drug containing a substance within the CSA’s definition of “marijuana” would need FDA approval to be lawfully “introduce[d] or deliver[ed] for introduction into interstate commerce,” unless an IND is in effect for that drug. See 21 U.S.C. 355(a), 355(i), 331(d). To date, although there have been INDs for drugs containing a substance within the CSA’s definition of “marijuana,” no such drugs have been approved by FDA.

DOJ is seeking comment on the practical consequences of rescheduling marijuana into schedule III under the relevant statutory frameworks.

Conclusion

Based on the legal opinion of OLC and consideration of the scientific and medical evaluation and accompanying recommendation of HHS, the Attorney General is initiating a rulemaking that proposes the placement of marijuana in schedule III of the CSA. DOJ is soliciting comments on this proposal.

X. Regulatory Analyses

1. *Executive Orders 12866 (Regulatory Planning and Review), 13563 (Improving Regulation and Regulatory Review) and 14094 (Modernizing Regulatory Review)*

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for removing a drug or other substance from the list of controlled substances. Such actions are exempt from review by the Office of Management and Budget pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563 and 14094.

While this scheduling action is exempt from review under Executive Order 12866, DOJ recognizes this action may have unique economic impacts. As stated above, marijuana is subject to a number of State laws that have allowed

a multibillion dollar industry to develop. DOJ acknowledges that there may be large impacts related to Federal taxes and research and development investment for the pharmaceutical industry, among other things. DOJ is specifically soliciting comments on the economic impact of this proposed rule. DOJ will revise this section at the final rule stage if warranted after consideration of any comments received.

2. Executive Order 12988 (Civil Justice Reform)

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

3. Executive Order 13132 (Federalism)

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the Federal Government and the States, or the distribution of power and responsibilities among the various levels of government.

4. Executive Order 13175 (Consultation and Coordination With Indian Tribal Governments)

This proposed rule does not have Tribal implications warranting the application of Executive Order 13175. This rule does not have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes.

5. Regulatory Flexibility Act

DOJ has concluded that this action may have a significant economic impact on a substantial number of small entities under the Regulatory Flexibility Act, 5 U.S.C. 601 *et seq.* For example, section 280E of the Internal Revenue Code bars businesses from claiming tax deductions for otherwise allowable expenses where the business “consists of trafficking in controlled substances (within the meaning of schedule I and II of the Controlled Substances Act).” 26 U.S.C. 280E. If marijuana is ultimately transferred to schedule III, section 280E would no longer serve as a statutory bar to claiming deductions for those expenses. In addition, small entities engaged in research on marijuana may

be subject to different research protocols set by DEA if the research is conducted on a schedule III substance rather than a schedule I substance.⁴¹ However, DOJ is currently not in a position to estimate the number of small entities affected by these or other potential effects of this action. DOJ seeks comment and additional information to inform its analysis.

6. *Unfunded Mandates Reform Act of 1995*

In accordance with the Unfunded Mandates Reform Act of 1995 (“UMRA”), 2 U.S.C. 1501 *et seq.*, DOJ has determined that this action would not result in any Federal mandate that may result “in the expenditure by State, local, and Tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any 1 year.” See 2 U.S.C. 1532(a). Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA.

7. *Paperwork Reduction Act of 1995*

This action does not impose any new or revised “collection[s] of information” as defined by the Paperwork Reduction Act of 1995, 44 U.S.C. 3502(3).

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is proposed to be amended as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

■ 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

■ 2. Amend § 1308.11 by:

■ a. Removing paragraphs (d)(23) and (58).

■ b. Redesignating paragraphs (d)(24) through (57) and (59) through (104) as paragraphs (d)(23) through (102), respectively.

■ c. Revising newly redesignated paragraph (d)(30).

The revision reads as follows:

§ 1308.11 Schedule I.

* * * * *

(d) * * *

⁴¹ See Drug Enforcement Admin., *Researcher's Manual 18–21* (2022), [https://www.deadiversion.usdoj.gov/GDP/DEA-DC-057\(E.O.-DEA217\)_Researchers_Manual_Final_signed.pdf](https://www.deadiversion.usdoj.gov/GDP/DEA-DC-057(E.O.-DEA217)_Researchers_Manual_Final_signed.pdf).

(30) Tetrahydrocannabinols—7370

(i) Meaning tetrahydrocannabinols, except as in paragraphs (d)(30)(ii) and (iii) of this section, naturally contained in a plant of the genus *Cannabis* (cannabis plant), as well as synthetic equivalents of the substances contained in the cannabis plant, or in the resinous extracts of such plant, or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity to those substances contained in the plant.

(ii) Tetrahydrocannabinols does not include any material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.

(iii) Tetrahydrocannabinols does not include any substance that falls within the definition of marijuana set forth in 21 U.S.C. 802(16).

* * * * *

■ 3. Amend § 1308.13 by adding paragraphs (h) through (j) to read as follows:

§ 1308.13 Schedule III.

* * * * *

(h) *Marijuana*. Marijuana, as defined in 21 U.S.C. 802(16).

(i) *Marijuana extract*. Marijuana extract, meaning an extract containing one or more cannabinoids that has been derived from any plant of the genus *Cannabis*, containing greater than 0.3 percent delta-9-tetrahydrocannabinol on a dry weight basis, other than the separated resin (whether crude or purified) obtained from the plant.

(j) *Naturally derived delta-9-tetrahydrocannabinols*. (1) Meaning those delta-9-tetrahydrocannabinols, except as in paragraphs (j)(2) and (3) of this section, that are naturally contained in a plant of the genus *Cannabis* (cannabis plant).

(2) Naturally derived delta-9-tetrahydrocannabinols do not include any material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.

(3) Naturally derived delta-9-tetrahydrocannabinols do not include any delta-9-tetrahydrocannabinols contained in substances excluded from the definition of marijuana as set forth in 21 U.S.C. 802(16)(B)(ii).

Dated: May 16, 2024.

Merrick B. Garland,
Attorney General.

[FR Doc. 2024–11137 Filed 5–17–24; 11:15 am]

BILLING CODE 4410–09–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 165

[Docket Number USCG–2024–0393]

RIN 1625–AA11

Regulated Navigation Area; Cuyahoga River, Cleveland, OH

AGENCY: Coast Guard, DHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Coast Guard is proposing to establish a temporary Regulated Navigation Area for certain waters of the Cuyahoga River. This action is necessary to provide for the safety of life on these navigable waters near the “Irishtown Bend” in Cleveland, Ohio, during a bank stabilization construction project from August 15, 2024, through November 30, 2025. This proposed rulemaking would limit vessel speeds near the area and prohibit vessels from being inside the Regulated Navigation Area during construction hours unless authorized by the Captain of the Port Sector Eastern Great Lakes or a designated representative. We invite your comments on this proposed rulemaking.

DATES: Comments and related material must be received by the Coast Guard on or before June 20, 2024.

ADDRESSES: You may submit comments identified by docket number USCG–2024–0393 using the Federal Decision-Making Portal at <https://www.regulations.gov>. See the “Public Participation and Request for Comments” portion of the

SUPPLEMENTARY INFORMATION section for further instructions on submitting comments. This notice of proposed rulemaking with its plain-language, 100-word-or-less proposed rule summary will be available in this same docket.

FOR FURTHER INFORMATION CONTACT: If you have questions about this proposed rulemaking, call or email Cody Mayrer at Marine Safety Unit Cleveland’s Waterways Management Division, U.S. Coast Guard; telephone 216–937–0111, email D09-SMB-MSUCLEVELAND-WWM@uscg.mil.

SUPPLEMENTARY INFORMATION:

I. Table of Abbreviations

CFR Code of Federal Regulations
DHS Department of Homeland Security
FR Federal Register
NPRM Notice of Proposed Rulemaking
§ Section
U.S.C. United States Code



70148

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(e) TVA's issuance of a permit does not mean that TVA has determined a facility or obstruction is safe for any purpose or that TVA has any duty to make such a determination. In issuing a permit, TVA assumes no liability to the applicant or to any third party for any damages to property or personal injuries arising out of or in any way connected with applicant's construction, operation, or maintenance of the permitted facility.

■ 3. Amend § 1304.100 by:

- a. Revising the seventh sentence; and
- b. Adding a sentence after the seventh sentence.

The revision and addition read as follows:

§ 1304.100 Scope and intent.

* * * Existing floating cabins may remain moored on the Tennessee River System provided they remain in compliance with the rules in this part and obtain a section 26a permit from TVA issued after October 12, 2021. Existing floating cabins that do not apply for a permit by the deadline in this part or do not remain in compliance with the rules in this part are subject to the removal provisions of this part and section 9b of the TVA Act. * * *

■ 4. Amend § 1304.101 by:

- a. Revising paragraph (c);
- b. Revising paragraph (h)(2) introductory text;
- c. Revising paragraph (h)(3); and
- d. Revising paragraph (i)(3).

The revisions read as follows:

§ 1304.101 Floating cabins

* * * * *

(c) All floating cabins shall comply with the rules contained in this part and make application for a section 26a permit by October 1, 2029. TVA may, at its sole discretion, deny an initial application for a floating cabin submitted after this date. Unpermitted structures are subject to the removal provisions of this part and Section 9b of the TVA Act.

* * * * *

(h) * * *

(2) Any alterations to the dimensions or approved plans for an existing floating cabin (monolithic frame or attached structure) shall be deemed a structural modification and shall require prior written approval from TVA. All expansions in length, width, or height are prohibited, except under the following circumstances if approved in writing in advance by TVA. Structural modifications to attached structures are subject to § 1304.101(i).

* * * * *

(3) Owners must submit an application to TVA sixty (60) days in

advance of proposed rebuilding of an entire or significant portion of a floating cabin (monolithic frame or attached structures). The owner shall not begin construction until prior written acknowledgment from TVA is received. Plans for removal of the existing floating cabin or portions to be rebuilt shall be acknowledged in writing by TVA before removal occurs, and the removal shall be at the owner's expense before construction of the rebuild may begin. The owner shall provide evidence of approval from the marina operator to rebuild within the approved harbor limits of a commercial marina. TVA may require a new permit for the proposed rebuilding. Construction of the rebuilt floating cabin must be completed within 18 months. The rebuilt monolithic frame of the floating cabin shall match the exact configuration and dimensions (length, width, and height) of both the total monolithic frame and the enclosed and open space as approved by TVA; attached structures are subject to § 1304.101(i). The footprint of the attached structures shall not be incorporated into the footprint of the monolithic frame of the floating cabin.

* * * * *

(i) * * *

(3) Attached structures shall not exceed 14 feet in height from the lowest floor level, shall not be enclosed, shall not be connected to the monolithic frame by a single roofline, and shall comply with § 1304.204(p).

* * * * *

■ 5. Amend § 1304.103 by:

- a. Revising paragraph (a);
- b. Revising paragraph (d); and
- c. Removing paragraph (e).

The revisions read as follows:

§ 1304.103 Health, safety, and environmental standards

(a) *Wastewater.* Floating cabins shall comply with § 1304.2(d) with regard to discharges into navigable waters of the United States. All discharges, sewage, and wastewater, and the pumping, collection, storage, transport, and treatment of sewage and wastewater shall be managed in accordance with all applicable federal, state, and local laws and regulations (satisfactory evidence of compliance to be provided to TVA upon request). Upon receipt of documentation that a floating cabin is in violation of any federal, state, or local discharge or water quality regulation by the respective regulatory agency or upon failure to provide satisfactory evidence of compliance at TVA's request, TVA is authorized to revoke the permit and require removal of the floating cabin from the Tennessee River System if the

violation is not corrected as specified by the regulatory agency in accordance with the agency's requirements or if satisfactory evidence of compliance is not provided to TVA.

* * * * *

(d) *Electrical.* Floating cabins shall comply with all applicable federal, state, and local laws and regulations regarding electrical wiring and equipment (satisfactory evidence of compliance to be provided to TVA upon request). Upon receipt of documentation that a floating cabin is in violation of any federal, state, or local electrical standard or regulation by the respective regulatory agency or upon failure to provide satisfactory evidence of compliance at TVA's request, TVA is authorized to revoke the permit and require removal of the floating cabin from the Tennessee River System if the violation is not corrected as specified by the regulatory agency in accordance with the agency's requirements or if satisfactory evidence of compliance is not provided to TVA. Floating cabins shall comply with § 1304.209(c)(2).

Michael McCall,

Vice President, Environment and Sustainability.

[FR Doc. 2024-19373 Filed 8-28-24; 8:45 am]

BILLING CODE 8120-08-P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1301

[Docket No. DEA-1362]

RIN 1117-AB77

Schedules of Controlled Substances:
Rescheduling of Marijuana

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of hearing on proposed rulemaking.

SUMMARY: This is notice that the Drug Enforcement Administration will hold a hearing with respect to the proposed rescheduling of marijuana into schedule III of the Controlled Substances Act. The proposed rescheduling of marijuana was initially proposed in a Notice of Proposed Rulemaking published in the *Federal Register* on May 21, 2024.

DATES: Interested persons desiring to participate in this hearing must provide written notice of desired participation as set out below, on or before September 30, 2024.

The hearing will commence on December 2, 2024, at 9 a.m. ET at 700

Army Navy Drive, Arlington, VA 22202. The hearing may be moved to a different place and may be continued from day to day or recessed to a later date without notice other than announcement thereof by the presiding officer at the hearing. 21 CFR 1316.53.

ADDRESSES: To ensure proper handling of notification, please reference “Docket No. DEA–1362” on all correspondence.

- *Electronic notification* should be sent to nprm@dea.gov.

- *Paper notification* sent via regular or express mail should be sent to Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Drug and Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362–3249. *Email:* nprm@dea.gov.

SUPPLEMENTARY INFORMATION:

Background

On May 21, 2024, the Department of Justice published a notice of proposed rulemaking (NPRM) to transfer marijuana from schedule I of the Controlled Substances Act (CSA) to schedule III of the CSA, consistent with the view of the Department of Health and Human Services (HHS) that marijuana has a currently accepted medical use, has a potential for abuse less than the drugs or other substances in schedules I and II, and that its abuse may lead to moderate or low physical dependence or high psychological dependence.¹ The CSA requires that such actions be made through formal rulemaking on the record after opportunity for a hearing. 21 U.S.C. 811(a).

The NPRM stated that if the transfer to schedule III is finalized, the regulatory controls applicable to schedule III controlled substances would apply, as appropriate, along with existing marijuana-specific requirements and any additional controls that might be implemented, including those that might be implemented to meet U.S. treaty obligations. If marijuana is transferred into schedule III, the manufacture, distribution, dispensing, and possession of marijuana would remain subject to the applicable criminal prohibitions of the CSA. Any drugs containing a substance within the CSA’s definition of “marijuana” would also remain subject to the applicable prohibition in the

Federal Food, Drug, and Cosmetic Act (FDCA).

The NPRM invited interested parties to submit requests for hearing on or before June 20, 2024. DEA received numerous requests for a hearing in response to the NPRM.

Upon review of the requests for a hearing, I am authorizing a hearing to be conducted in accordance with the Administrative Procedure Act (5 U.S.C. 551–559), the CSA (21 U.S.C. 811, *et seq.*) and the DEA regulations.

Hearing Notification

Pursuant to 21 U.S.C. 811(a) and 21 CFR 1308.41, DEA will convene a hearing on the NPRM. The hearing will commence on December 2, 2024, at 9 a.m. ET at the DEA Hearing Facility, 700 Army Navy Drive, Arlington, VA 22202. The hearing will be conducted pursuant to the provisions of 5 U.S.C. 556 and 557, and 21 CFR 1308.41–1308.45, and 1316.41–1316.68. DEA is committed to conducting a transparent proceeding. Regarding the methods of public access, DEA will provide updates on the DEA website, <https://www.dea.gov>.

In accordance with 21 U.S.C. 811 and 812, the purpose of the hearing is to “receiv[e] factual evidence and expert opinion regarding” whether marijuana should be transferred to schedule III of the list of controlled substances. 21 CFR 1308.42.

Every interested person (defined in 21 CFR 1300.01(b) as “any person adversely affected or aggrieved by any rule or proposed rule issuable” under 21 U.S.C. 811), who wishes to participate in the hearing shall file a written notice of intention to participate for review by the Agency. Electronic filing may be made as a PDF attachment via email to the Drug Enforcement Administration, Attn: Administrator at nprm@dea.gov, on or before 11:59 p.m. Eastern Time on September 30, 2024. If filing by mail, written notice must be filed with the Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, VA 22152, and must be postmarked on or before September 30, 2024. Paper requests that duplicate electronic submissions are not necessary and are discouraged.

Each notice of intention to participate must conform to 21 CFR 1308.44(b) and in the form prescribed in 21 CFR 1316.48. Among those requirements, such requests must:

- (1) State with particularity the interest of the person in the proceeding;
- (2) State with particularity the objections or issues concerning which the person desires to be heard; and

(3) State briefly the position of the person regarding the objections or issues.

Any person who has previously filed a request for hearing or to participate in a hearing need not file another request; the request for hearing is deemed to be a notice of appearance under 21 CFR 1308.44(b).

After the deadline to request to participate in the hearing, I will assess the notices submitted and make a determination of participants. Following that assessment, I will designate a presiding officer to preside over the hearing. The presiding officer’s functions shall commence upon designation, as provided in 21 CFR 1316.52. The presiding officer will have all powers necessary to conduct a fair hearing, to take all necessary action to avoid delay, and to maintain order. *Id.* The presiding officer’s authorities include the power to hold conferences to simplify or determine the issues in the hearing or to consider other matters that may aid in the expeditious disposition of the hearing; require parties to state their position in writing; sign and issue subpoenas to compel the production of documents and materials to the extent necessary to conduct the hearing; examine witnesses and direct witnesses to testify; receive, rule on, exclude, or limit evidence; rule on procedural items; and take any action permitted by the presiding officer under DEA’s hearing procedures and the APA. *Id.*

Comments on or objections to the proposed rule submitted under 21 CFR 1308.43(g) will be offered as evidence at the hearing, but the presiding officer shall admit only evidence that is competent, relevant, material, and not unduly repetitive. 21 CFR 1316.59(a).

Anne Milgram,
Administrator.

[FR Doc. 2024–19370 Filed 8–26–24; 4:45 pm]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Alcohol and Tobacco Tax and Trade Bureau

27 CFR Part 9

[Docket No. TTB–2024–0004; Notice No. 233]

RIN 1513–AC98

Proposed Establishment of the Rancho Guejito Viticultural Area

AGENCY: Alcohol and Tobacco Tax and Trade Bureau, Treasury.

¹ *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 FR 44597 (May 21, 2024).

September 26, 2024

Drug Enforcement Administration
Attn: Hearing Clerk/OALJ
8701 Morrisette Drive
Springfield, VA 22152.
Subject: Docket No. DEA-1362, Request for Participation

Dear Sir or Madam:

Doctors for Drug Policy Reform (the “Organization”) and the undersigned, Bryon Adinoff, M.D., hereby requests to participate in the matter of “Schedules of Controlled Substances: Rescheduling of Marijuana” (89 Fed. Reg. 44597).¹

I. Introduction

Doctors for Drug Policy Reform, or D4DPR (formerly known as Doctors for Cannabis Regulation) supports removing cannabis in all its forms from the Controlled Substances Act. In the context of the proposed rule, however, it is the Organization’s position that the medical, scientific, and other evidence supports a Schedule V (alternatively, schedule IV) classification for “marijuana,” “marijuana extract,” and “naturally derived delta-9-tetrahydrocannabinols” and requests to participate in same in support of its position.

First, the Organization agrees that marijuana has a currently accepted medical use in treatment in the United States and should be removed from Schedule I. As the premier organization of health professionals and scientists specifically organized to provide expert evidence related to the responsible regulation of cannabis, the Organization is best positioned to present additional evidence to support that assessment and to contextualize evidence and argument to the contrary.

Second, while the Organization agrees with HHS that marijuana should be removed from Schedule I, it contends that the evidence, properly considered, supports a classification below Schedule III. Relative to substances in Schedule III and Schedule IV, marijuana has a low potential for abuse and lower psychological/physical dependence.² In support of its position, the Organization intends to present fact and expert testimony/opinion from two of its members with relevant expertise, Drs. Bryon Adinoff and David Nathan, and whose CVs/bios are attached. The HHS analysis failed to fully and properly evaluate the relative abuse potential and psychological/physical dependence of marijuana abuse compared to Schedule III, IV, and V drugs, even though the statute requires this analysis and prior scheduling actions involving other drugs

¹ The Organization previously submitted a request for hearing. For good measure, it also offers this submission.

² The Organization notes that “abuse,” “dependence,” and marijuana are terms in the statute. The use of statutory terms herein indicates no agreement on the propriety of their use in other contexts. For example, “drug abuse” is no longer a diagnosis in DSM-V and therefore, abuse should not be used by medical professionals.

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have done it too. At the requested hearing, the Organization intends to provide testimony and evidence on this matter to assist the agency in its final determination.

The Organization also seeks to offer testimony on the issue of the meaning and application of the statutory term “abuse,” particularly as it relates to cannabis use. Both FDA and DEA in the past have applied a definition of “drug abuse” as the intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desired psychological or physiological effect.”³ Accordingly, “abuse potential” abuse potential refers to “the likelihood that abuse will occur with a particular drug product or substance with CNS activity.”

These definitions, however, are not generally accepted by the medical profession. Rather, drug or substance abuse, as used in the statute, should be understood to capture use or excessive use of a drug in a way that is harmful or detrimental to self, society, or both.⁴ This difference is particularly important in assessing the research and epidemiological evidence. A drug like cannabis that is widely available is often used without a prescription but not in a way that is harmful. Indeed, there is currently no way to “prescribe” cannabis, so all cannabis use is used without a prescription.

The Administrative Procedure Act provides “as the orderly conduct of public business permits, an interested person may appear before an agency or its responsible employees for the presentation, adjustment, or determination of an issue, request, or controversy in a proceeding, whether interlocutory, summary, or otherwise, or in connection with an agency function.” 5 U.S.C. § 555(b). It similarly provides that the “agency as a matter of policy shall provide for the exclusion of irrelevant, immaterial, or unduly repetitious evidence.” 5 U.S.C. § 556.

Because the Organization would adversely affected by the proposed rule, has interests that differ from other potential participants, intends to provide non-cumulative evidence to assist the agency’s final determination, and is well-suited to cross-examine evidence put forward by industry and rescheduling opponents alike, it requests a rulemaking hearing or to participate in same in support of its position.⁵

³ See, for example, <https://www.fda.gov/media/116739/download>.

⁴ The legislative history and agency precedent indicates that a determination that “potential for abuse” should not “be determined on the basis of isolated or occasional nontherapeutic purposes,” but rather “there must exist a substantial potential for the occurrence of significant diversions from legitimate channels, significant use by individuals contrary to professional advice, or substantial capability of creating hazards to the health of the user or the safety of the community.” 76 Fed. Reg. 77330 at 336. Based on this definition, not all cannabis use, whether medicinal or recreational, would constitute abuse.

⁵ See *Animal Legal Defense Fund, Inc. v. Vilsack*, 237 F. Supp. 3d 15, 22-23 (D.D.C. 2017) (citing *Nichols v. Bd. of Trustees of Asbestos Workers Local 24 Pension Plan*, 835 F.2d 881, 896-97 (D.C. Cir. 1987)).

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II. Interests of the person in the proceeding.

The Organization is a 501(c)(3) non-profit organization that serves as a global voice for licensed health professionals and scientists advocating for evidence-based drug policies and best practices that advance public health, reduce stigma, and minimize harm. Its website is located at <https://www.d4dpr.org/>.

In 2015, Dr. David Nathan founded the Organization as Doctors for Cannabis Regulation to bridge the gap between the policy of prohibition and the unregulated legalization of cannabis. The Organization has been dedicated to that mission ever since. Since that time, it has served as the premier national physicians' association committed to the responsible regulation of cannabis in the United States and abroad, a global advocate, and represents the voices of over 400 physicians and licensed medical practitioners, in support of evidence-based cannabis regulation and legalization. The Organization is comprised of doctors, nurses, pharmacists—many if not nearly all of whom are registrants.

The Organization is frequently called upon to provide expert testimony in significant legislative and administrative contexts unaffiliated with the cannabis industry. It provided testimony for the first-ever Congressional subcommittee hearing on cannabis legalization and on dozens state-level initiatives and bills pertaining to medical and adult-use cannabis. The Organization frequently collaborates with other advocacy groups to educate the public, including on rescheduling. The Organization is not affiliated with the cannabis industry.

As noted on its website, the Organization also offers curriculums on cannabis education, each of which has been carefully vetted by our D4DPR Board and Experts.

The Organization and its members not only have a particularized interest and are affected by the proposed rule, but are in the best position to provide relevant, material, and not unduly repetitious evidence sought by the agency.⁶

III. Objections or issues concerning which the person desires to be heard.

As an organization of health care professionals and scientists formed years ago to bridge the gap between the policy of prohibition and the unregulated legalization of cannabis, the Organization is generally interested in participating a hearing central to its longstanding mission.

⁶ The Organization and its members are also interested parties considering the differences between Schedule III and Schedule V substances, for example, in dispensing limits for prescriptions. 21 U.S.C. § 829. These differences directly members of the Organization. The Organization further notes that rescheduling (even from I to III) could adversely impact its members because it may affect how medical marijuana is recommended/prescribed or dispensed, which at present, is done based on recommendations and not prescriptions due to its Schedule I status.

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The Organization's participation will ensure that the evidence presented by both industry and rescheduling opponents alike are placed in the proper medical and scientific context.

In addition to general participation, as to specific and particularized issues of interest to the Organization, the Organization wishes to be heard on the following two issues.

- a. **Physical and psychological dependence *relative* to Schedule III, IV, and V compounds and relative potential for abuse.** The HHS recommendation states that marijuana was compared to controlled substances in schedule III (ketamine) and schedule IV (benzodiazepines, zolpidem, and tramadol), as well as to other schedule II substances (fentanyl and hydrocodone). Without much additional explanation, the recommendation states that it “evaluated the totality of the available data and have concluded that it supports the placement of marijuana in Schedule III.” It is unclear, however, whether and how HHS performed a relative potential for abuse and dependence analysis compared to Schedule III and IV substances.
- b. **The meaning of “abuse” / “abuse potential” and its application to marijuana.** Historically, FDA and/or DEA has defined “drug abuse” as the intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desired psychological or physiological effect.” But this definition or concept is not generally accepted in the medical community, and what constitutes abuse with a culturally available and sanctioned substance cannot be based on whether, on occasion, an individual consumes the substance on their own initiative rather than based on medical advice. Just like few would consider having a glass of wine with dinner to be alcohol abuse, few medical professionals would seriously consider smoking marijuana once a week on Friday to relax after work to be “abuse.” The definition of “abuse” and “abuse potential” is important because it undergirds the HHS findings with respect to marijuana’s “potential for abuse.” Properly considered, marijuana does not have a “potential for abuse” any greater than drugs in the benzodiazepine class (Schedule IV).

IV. Brief Statement on the Issues.

- a. **Physical and psychological dependence *relative* to Schedule III, IV, and V compounds and relative potential for abuse.** The HHS recommendation does not appear to do a meaningful comparative analysis in assessing scheduling factor three, even though the statute demands that in determining a final scheduling placement among Schedules III, IV, or V, the agency must compare physical and psychological dependence among them.⁷ Notably, both agencies have done this analysis in the past.

⁷ For example, Schedule III, factor 3 (21 U.S.C. § 812(b)(3)(C)) is “Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence,” while Schedule IV, factor 4 (21 U.S.C. § 812(b)(4)(C)) is “Abuse of the drug or other

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For example, the agency concluded in 2013 that Lorcaserin should be placed in Schedule IV (78 Fed. Reg. 26701), based on an abuse potential study comparing lorcaserin to zolpidem (Schedule IV) and ketamine (Schedule III). The agency concluded in 2005 that pregabalin warranted Schedule V placement because “withdrawal effects of pregabalin are less severe than with other substances currently controlled in Schedule IV.” (70 Fed. Reg. 43633.)

The HHS analysis on relative abuse potential, reproduced below, is hard to understand:

[T]he rank order of these substances regarding harms does not consistently align with the relative scheduling placement of these drugs in the CSA due to the pharmacological differences between various classes of drugs.

*There are a number of confounding factors that likely influence the adverse outcomes measured in various epidemiological databases and account for the rank ordering of the drugs evaluated on these measures. For example, each substance has associated with it a different population that abuse that substance, a different prevalence of abuse, and a different profile of severe adverse outcomes in a setting of nonmedical use and abuse. Thus, it is challenging to reconcile the ranking of relative harms associated with the comparators used in this evaluation when the rankings differ across various epidemiological databases, and when these rankings often do not align with the scheduling placement of these comparators under the CSA. **To address these challenges, we evaluated the totality of the available data and have concluded that it supports the placement of marijuana in Schedule III.***

The Organization does not believe this analysis is sufficient, and it intends to provide detailed testimony from two witnesses on the low physical and psychological dependence of cannabis relative to Schedule III and IV substances.⁸ In particular, the analysis does not properly compare cannabis to the benzodiazepine class in Schedule IV, and it is well documented that benzodiazepine abuse results in significant physiological and psychological dependence. The proposed rule similarly recognizes that the public health risk of benzodiazepines is substantially greater than the risk presented by cannabis. The evidence will show that compared to benzodiazepines, abuse of marijuana leads to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.

substance may lead to limited physical dependence or psychological dependence *relative to the drugs or other substances in schedule III.*” To determine whether a drug properly is placed in Schedule III or IV, it is therefore necessary to consider the relative dependence of the substance compared to other substances in Schedule III. The same can be said of Schedules IV and V.

⁸ One witness has recognized expertise in addiction and substance use disorders. The other has expertise in cannabis policy and psychiatry.

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b. The meaning of “abuse” / “abuse potential” and its application to marijuana.

Marijuana, like most drugs, can be “abused.” But what constitutes “abuse” in the context of a culturally available and state-regulated substance cannot be based simply on whether, on occasion, an individual consumes the substance on their own initiative rather than based on medical advice, without any harm to the individual. Few would consider a glass of wine with dinner to be alcohol “abuse.” Likewise, occasional marijuana consumption that presents no individual or societal harm is not “abuse.” The proposed rule recognizes that “the vast majority of individuals who use marijuana are doing so in a manner that does not lead to dangerous outcomes to themselves or others.” None of that is “abuse,” and in assessing prevalence as part of a potential for abuse assessment, DEA should neither include medical uses of marijuana nor non-problematic non-medical uses.

All notices to be sent pursuant to the proceeding should be addressed to:

Bryon Adinoff
812 S Gaylord St
Denver, CO 80209

David L. Nathan, MD, DFAPA
Princeton Psychiatry & Consulting, LLC
601 Ewing Street, Suite C-10
Princeton, NJ 08540

and

Matthew C. Zorn
Yetter Coleman LLP
811 Main Street, Ste. 4100
Houston, TX 77002

Respectfully yours,

A handwritten signature in black ink, appearing to read 'B. Adinoff', written in a cursive style.

Bryon Adinoff, M.D.
President, Doctors for Drug Policy Reform

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

PRELIMINARY ORDER

I am the Administrative Law Judge (ALJ) designated by the Administrator of the Drug Enforcement Administration (DEA or Agency) to hear this case.

On May 21, 2024, the United States Department of Justice (DOJ) through the DEA issued a notice of proposed rulemaking (NPRM) proposing to transfer marijuana from Schedule I of the Controlled Substances Act (CSA) to Schedule III. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 44597, 44597 (2024). In an order dated August 29, 2024 (General Notice of Hearing or GNoH), the DEA Administrator determined that in-person hearing proceedings are appropriate and fixed a December 2, 2024 commencement date at the DEA Hearing Facility. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 70148, 70148-49 (2024).

The NPRM directed, *inter alia*, that “[a]ll requests for a hearing and waivers, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with DEA.” 89 Fed. Reg. at 44598. The General Notice of Hearing acknowledged the regulatory requirement that under the DEA regulations, an “interested person” is “any person adversely affected or aggrieved by any rule or proposed rule issuable under 21 U.S.C. § 811.” 89 Fed. Reg. at 70149. The GNoH instructed any person seeking to participate in the rescheduling hearing to submit a filing:

- (1) Stat[ing] with particularity with interest of the person in the proceeding;
- (2) Stat[ing] with particularity the objections or issues concerning which the person desires to be heard; and
- (3) Stat[ing] briefly the position of the person regarding the objections or issues.

Id.

On October 29, 2024, two letters from the DEA Administrator were hand-carried to the DEA Office of Administrative Law Judges. Attachments 1, 2. One letter (the Participant Letter or PL)¹ designated a list of twenty-five “participants” (Designated Participants or DPs), and the other, by its terms, directed the utilization of livestreaming throughout the hearing proceedings (the Livestream Letter or LSL).² The PL and LSL have been attached to this order as the record has no indication as to whether either or both documents were served on the Designated Participants or any of those who sought to be DPs.

Although the Participant Letter designated a list of enumerated entities and individuals as DPs, there is no indication in the four corners of the document as to whether the “participants” support or oppose the NPRM or how the “participants” satisfy the “interested person” definition set forth in the regulations. 21 C.F.R. §§ 1300.01(b), 1308.44(a)-(b). Indeed, the PL contains only a list of persons and organizations accompanied by one or more email addresses, without the benefit of notices of appearance, addresses, or even phone numbers. While the NPRM directed that the Office of Administrative Law Judges be served with a courtesy copy of any hearing request filing(s),³ the GNoH contained no such requirement. Thus, this tribunal is not in possession of documentation related to whether/how the Designated Participants would be “adversely affected or aggrieved” by the proposed regulation change in the NPRM,⁴ or any other particularly helpful information. The regulatory language regarding the requirement that only “interested person[s]” may request (and by implication be designated with) hearing participant status is not permissive in nature. 21 C.F.R. § 1308.44. Equally directive is the language in the regulations that requires that an “interested person” demonstrate that he/she/it would be “adversely affected or aggrieved” by the proposed scheduling action. 21 C.F.R. § 1300.01(b).

In granting the Attorney General (and by delegation the DEA Administrator⁵) authority to schedule or reschedule any substance, Congress required that such an action “shall be made on the record after [an] opportunity for a hearing pursuant to the rulemaking procedures prescribed by the [Administrative Procedure Act (APA)].” 21 U.S.C. § 811(a). Under the APA, “the

¹ Attachment 1.

² Attachment 2.

³ 89 Fed. Reg. at 44598.

⁴ Indeed, the Agency has furnished this tribunal with no correspondence from itself or the Designated Participants that was generated in response to the GNoH.

⁵ 28 C.F.R. § 0.100.

proponent of a[n] . . . order has the burden of proof.”⁶ 5 U.S.C. § 556(d); *see also* 21 C.F.R. § 1316.56 (“[a]t any hearing, the proponent for the issuance, amendment, or repeal of any rule shall have the burden of proof.”). Thus, just as the Agency carries the burden of proof to prevail on its proposed rulemaking, those among the Designated Participants seeking active participation in this hearing must establish that they have made timely application and are eligible as an “interested person.” To the extent that any of this has been done or adjudicated, it is not transparent in the present record. The record currently contains no hearing requests, notices of appearance, or correspondence between the Agency and the Designated Participants or those who sought that status. As the record currently stands, although the Agency has fixed a December 2, 2024 hearing date, there is no way to discern from the present record which DPs support or oppose the NPRM. To effectively preside over this hearing, additional information must be furnished to the tribunal forthwith.

Accordingly, it is herein **ORDERED** that any Designated Participant listed in the Participant Letter who seeks active participation in these hearing proceedings shall, no later than **2:00 P.M. Eastern Time (ET) on November 12, 2024**, file with this tribunal a *brief* notice which will include the following information/document(s): (1) the name, address, phone number, and general nature/principal mission of the DP’s practice, profession, or business; (2) a notice of appearance for the counsel(s) of record that will be representing the DP at the hearing; (3) the date that a request for hearing and/or participation was properly filed by the DP with the DEA; (4) why/how the DP would be sufficiently “adversely affected or aggrieved” by the proposed scheduling action to qualify as an “interested person” under the regulations;⁷ (5) whether the DP supports or opposes the rescheduling action the DEA seeks in its NPRM; and (6) any *known* conflicts of interest with DEA or DOJ leadership or personnel that may require disclosure.⁸

It is further **ORDERED** that the Government, shall, no later than **2:00 P.M. ET on November 12, 2024**, file with this tribunal a notice of appearance for its counsel(s) of record

⁶ The APA definition of “order” includes “the whole *or part* of a final disposition” 5 U.S.C. § 551(6) (emphasis supplied).

⁷ 21 C.F.R. §§ 1300.01(b), 1308.44(a)-(b).

⁸ In this regard, the PL identifies the International Association of Chiefs of Police (IACP) as a Designated Participant. My spouse is currently an administrative employee of that organization who has no management responsibilities. She has had no role in any IACP discussions regarding the issues to be adjudicated in these proceedings. That my spouse is an IACP employee will not affect my consideration of any evidence presented by or against IACP, nor will it influence in any way the ultimate recommendation that I make in this case to the DEA Administrator.

who will be appearing in these proceedings, as well as any *known* conflicts of interest that may require disclosure.

It is further **ORDERED**, that pursuant to the Administrator's General Notice of Hearing, preliminary hearing proceedings will commence at **9:30 ET on December 2, 2024** at the **DEA Hearing Facility, North Courtroom, 700 Army Navy Drive, Arlington, Virginia, 22202**. No testimony or other evidence will be received at this preliminary hearing, but those Designated Participants who will participate will come prepared with January-February 2025 availability dates regarding their counsel and any witness⁹ such DP will seek to present at the hearing on the merits. Dates for the hearing on the merits and other deadlines will be fixed in a prehearing ruling,¹⁰ which will be issued after the preliminary hearing where the parties have been afforded the opportunity to supply logistical and availability input.¹¹

It is further **ORDERED** that all proceedings will be governed by the provisions of 21 C.F.R. §§ 1316.41-1316.68.¹² Your attention is specifically directed to 21 C.F.R. § 1316.45, which provides, *inter alia*, that “[d]ocuments shall be dated and deemed filed upon receipt by the Hearing Clerk.” Documents (other than proposed exhibits¹³) will be filed electronically or by hardcopy. Only one method of document filing may be utilized.

Electronic Filing: The preferred method of filing correspondence in these proceedings is as a PDF attachment via email to the DEA Judicial Mailbox (**ECF-DEA@dea.gov**). The forwarding email on all electronically filed correspondence must indicate that it was simultaneously served on the Government and all DPs via email. The DPs must ensure that all

⁹ Given the potential number of anticipated participants, each participant, other than the Government (the burdened party in these proceedings), can generally expect to present the testimony of no more than one witness, with the opportunity to file written briefs at the conclusion of the hearing.

¹⁰ 21 C.F.R. § 1316.55.

¹¹ The courtrooms at the DEA Hearing Facility are spacious and modern, but not unlimited. Accordingly, in view of the potentially high number of hearing participants, it is anticipated that admission to the preliminary hearing will be limited to representatives (no more than two, preferably one) and credentialed media as designated by the Agency. See Attachment 2 at 1. The Administrator's directive in the LSL regarding livestreaming will afford those physically outside the courtroom an opportunity to observe the proceedings. *Id.* Naturally, witnesses will be admitted to the courtroom to testify at the merits hearings at times where their testimony is scheduled. No cell phone use by anyone will be permitted in the courtroom at any hearing conducted in this matter. The highest level of decorum will be maintained at all times during all hearings, and court attire is required for anyone participating in any capacity. All representative appearances will be live (not virtual) throughout, and all representatives must plan to arrive sufficiently early to allow security processing through the DEA Visitor Center, which is collocated with the DEA Hearing Facility at 700 Army Navy Drive, Arlington, Virginia, 22202.

¹² Additional helpful information regarding DEA administrative proceedings may be found at the OALJ website, <https://www.dea.gov/administrative-law-judges>.

¹³ The prehearing ruling issued after the preliminary hearing will supply direction on the manner in which exhibits may be filed with the tribunal.

documents filed with the DEA Judicial Mailbox are simultaneously served on the Government Mailbox at (dea.registration.litigation@dea.gov) and all other DPs. Any request(s) to modify email addresses of a party or counsel must be made on notice to this tribunal and all other parties. The email receipt date reflected by the DEA Judicial Mailbox server shall conclusively control all issues related to the date of service of all filed correspondence, provided however, that correspondence received after 5:00 p.m., local Washington, D.C. time, will be deemed to have been received on the following business day.

Hardcopy: Alternatively, correspondence may be filed in hardcopy form. Hardcopy filings must be served in triplicate and addressed to my attention at: **The DEA Office of Administrative Law Judges, 8701 Morrisette Drive, Springfield, Virginia 22152**. Because the DEA Hearing Facility is not physically collocated with the DEA mailing address, hardcopy filings must be posted sufficiently in advance of the due date to assure timely receipt by this office.

It is further **ORDERED** that any request for a continuance or for an extension of time to file a document must be made by written motion sufficiently in advance of scheduled deadline(s) to be considered and ruled upon.

Dated: October 31, 2024

JOHN

MULROONEY

JOHN J. MULROONEY, II
Chief Administrative Law Judge

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JOHN MULROONEY
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CERTIFICATE OF SERVICE

This is to certify that the undersigned, on October 31, 2024, caused a copy of the foregoing to be delivered to the following recipients: (1) James Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington for Village Farms International, via email at spennington@porterwright.com; (4) Aaron Smith for National Cannabis Industry Association, via email at aaron@thecannabisindustry.org and michelle@thecannabisindustry.org; (5) Chad Kollas for American Academy of Hospice and Palliative Medicine, via email at wchill@aahpm.org; (6) John Jones for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (7) Robert Head for Hemp for Victory, via email at robert@bluecordfarms.com; (8) Erin Gorman Kirk for the State of Connecticut, via email at erin.kirk@ct.gov; (9) Ellen Brown for Massachusetts Cannabis Advisory Board, via email at ellen@greenpathtraining.com; (10) Shanetha Lewis for Veterans Initiative 22, via email at info@veteransinitiative22.com; (11) Jason Castro for The Doc App. Db, My Florida Green, via email at jasoncastro@myfloridagreen.com; (12) Katy Green for The Commonwealth Project, via email at kag@platinumadvisors.com; (13) Ari Kirshenbaum for Saint Michael's College, via email at mslade@cannabispublicpolicyconsulting.com; (14) Jo McGuire for National Drug and Alcohol Screening Association, via email at jomcguire@ndasa.com; (15) Patrick Philbin for Smart Approaches to Marijuana, via email at pphilbin@torridonlaw.com; (16) Roneet Lev for International Academy on the Science and Impact of Cannabis, via email at roneetlev@gmail.com; (17) David Evans for Cannabis Industry Victims Educating Litigators, via email at thinkon908@aol.com; (18) Kenneth Finn, via email at kfinn@springsrehab.net; (19) Jennifer Homendy for National Transportation Safety Board, via email at executivesecretariat@ntsb.gov and correspondence@ntsb.gov; (20) Phillip Drum, via email at phillipdrum@comcast.net; (21) Attorney General Mike Hilgers for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (22) International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (23) Drug Enforcement Association of Federal Narcotics Agents, via email at marshallfisher@rocketmail.com; (24) Natalie P. Hartenbaum for American College of Occupational and Environmental Medicine, via email at occumedix@comcast.net and craig@acoem.org; (25) Sue Thau for Community Anti-Drug Coalitions of America, via email at cdoarn@cadca.org; (26) Tennessee Bureau of Investigation, via email at kim.litman@tbi.tn.gov; and (27) National Sheriff's Association, via email at sheriffs Skinner@collincountytx.gov and ykaraman@sheriffs.org.

**QUINN
FOX**

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by QUINN FOX
Date: 2024.10.31
15:20:05 -04'00'

Quinn Fox
Staff Assistant to the Chief Judge
Office of Administrative Law Judges

Attachment 1



U.S. Department of Justice
Drug Enforcement Administration

Office of the Administrator

Springfield, VA 22152

October 28, 2024

Hon. John J. Mulrooney, II
Chief Administrative Law Judge
Office of Administrative Law Judges
8701 Morrisette Drive
Springfield, VA 22152

Dear Chief Judge Mulrooney,

On May 21, 2024, the Department of Justice published a notice of proposed rulemaking (NPRM) to transfer marijuana from schedule I of the Controlled Substances Act (CSA) to schedule III of the CSA. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 44597 \(May 21, 2024\)](#). Upon review of the requests for hearing on the NPRM, I authorized a hearing to be conducted in accordance with the Administrative Procedure Act (APA), the CSA, and the Drug Enforcement Administration (DEA) regulations. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 70148 \(Aug. 29, 2024\)](#).

Pursuant to my authority under the CSA and DEA regulations, I reviewed the requests for a hearing under [21 CFR 1308.44\(a\)](#) and [1316.47](#), and the requests to participate under [21 CFR 1308.44\(b\)](#) and [1316.48](#), and I have determined that the following will be participants at the hearing:

1. Village Farms International Inc.
Shane Pennington of Porter Wright, spennington@porterwright.com
2. National Cannabis Industry Association
Aaron Smith, CEO and Co-Founder, and Michelle Rutter Friberg, Director of Government Relations, aaron@thecannabisindustry.org and michelle@thecannabisindustry.org
3. American Academy of Hospice and Palliative Medicine
Dr. Chad Kollas, MD, wchill@aahpm.org
4. Cannabis Bioscience International Holdings
John Jones, Treasurer and Director, ir@cbih.net

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OFFICE OF ADMINISTRATIVE
LAW JUDGES

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5. Hemp for Victory
Robert Head, Dr. Corey Burchman, Dr. Darinia Douchi, and Victor Bohm,
robert@bluecordfarms.com
 6. Cannabis Ombudsman, State of Connecticut
Erin Gorman Kirk, Erin.Kirk@ct.gov
 7. Massachusetts Cannabis Advisory Board
Ellen Brown, Research Subcommittee Chair, ellen@greenpathtraining.com
 8. Veterans Initiative 22
Shanetha Lewis, Executive Director, info@veteransinitiative22.com
 9. The Doc App. Db, My Florida Green
Nicholas Garulay, President and CEO, and Jason Castro, Inhouse Counsel,
jasoncastro@myfloridagreen.com
 10. The Commonwealth Project
Katy Green, kag@platinumadvisors.com
 11. Saint Michael's College
Ari Kirshenbaum, PhD, Professor of Psychology,
mslade@cannabispolicyconsulting.com
 12. National Drug and Alcohol Screening Association (NDASA)
Jo McGuire, jomcguire@ndasa.com
 13. Smart approaches to Marijuana (SAM)
Patrick Philbin, pphilbin@torridonlaw.com
 14. International Academy on the Science and Impact of Cannabis
Roneet Lev, roneetlev@gmail.com
 15. Cannabis Industry Victims Educating Litigators
David Evans, Sr. Counsel, thinkon908@aol.com
 16. Kenneth Finn, MD, kfinn@springsrehab.net
 17. National Transportation Safety Board (NTSB)
Jennifer Homendy, Chair, ExecutiveSecretariat@ntsb.gov and
correspondence@ntsb.gov
 18. Phillip Drum, Pharm D, phillipdrum@comcast.net

19. State of Nebraska
Attorney General Mike Hilgers, zachary.viglianco@nebraska.gov
20. International Association of Chiefs of Police (IACP)
voegtlin@theiacp.org
21. Drug Enforcement Association of Federal Narcotics Agents (DEAFNA)
marshallfisher@rocketmail.com
22. American College of Occupational and Environmental Medicine (ACOEM)
Natalie P. Hartenbaum, occumedix@comcast.net cc: craig@acoem.org
23. Community Anti-Drug Coalitions of America (CADCA)
Sue Thau, cdoarn@cadca.org
24. Tennessee Bureau of Investigation (TBI)
kim.litman@tbi.tn.gov
25. National Sheriff's Association
sheriffskinner@collincountytx.gov and ykaraman@sheriffs.org

Further, an Administrative Law Judge (ALJ) is now designated to preside over the hearing. The ALJ's functions commence upon this designation. *See* [21 CFR 1316.52](#). The designated ALJ will have powers necessary to conduct a fair hearing, to take all necessary action to avoid delay, and to maintain order. *Id.* The ALJ's authorities include the power to hold conferences to simplify or determine the issues in the hearing or to consider other matters that may aid in the expeditious disposition of the hearing; require parties to state their position in writing; sign and issue subpoenas to compel the production of documents and materials to the extent necessary to conduct the hearing; examine witnesses and direct witnesses to testify; receive, rule on, exclude, or limit evidence; rule on procedural items; and take any action permitted by the presiding officer under DEA's hearing procedures and the APA. *Id.*

Sincerely,



Anne Milgram
Administrator

Attachment 2



U.S. Department of Justice
Drug Enforcement Administration

Office of the Administrator

Springfield, VA 22152

October 28, 2024

Hon. John J. Mulrooney, II
Chief Administrative Law Judge
Office of Administrative Law Judges
8701 Morrisette Drive
Springfield, VA 22152

Dear Chief Judge Mulrooney,

On May 21, 2024, the Department of Justice published a notice of proposed rulemaking (NPRM) to transfer marijuana from schedule I of the Controlled Substances Act (CSA) to schedule III of the CSA. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 44597 \(May 21, 2024\)](#). Upon review of the requests for hearing on the NPRM, I authorized a hearing to be conducted in accordance with the Administrative Procedure Act (APA), the CSA, and the Drug Enforcement Administration (DEA) regulations. See [Schedules of Controlled Substances: Rescheduling of Marijuana, 89 FR 70148 \(Aug. 29, 2024\)](#).

On October 28, 2024, I designated an Administrative Law Judge (ALJ) to preside over the hearing. Given the public interest in this matter and DEA's commitment to conducting a transparent proceeding, I am exercising my inherent authority under [21 CFR 1307.03](#) to waive [21 CFR 1316.52](#) to the extent necessary to direct that the hearing be livestreamed. I am also exercising my authority to allow the in-person attendance of a limited number of credentialed media, as determined by DEA's Office of Public Affairs.

Sincerely,

Anne Milgram
Administrator

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OFFICE OF ADMINISTRATIVE
LAW JUDGES

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

ORDER REGARDING STANDING, SCOPE, AND PREHEARING PROCEDURES**On Standing**

The United States Department of Justice (DOJ) through the Drug Enforcement Administration (DEA or Agency) has initiated rulemaking proceedings to reschedule marijuana from Schedule I of the Controlled Substances Act (CSA) to Schedule III. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 44597, 44597 (2024). In another order (General Notice of Hearing or GNoH) published in the Federal Register, the DEA Administrator (the Administrator) subsequently determined that hearing procedures are appropriate and fixed a December 2, 2024 hearing commencement date. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 70148, 70148-49. Subsequent correspondence by the Administrator listed twenty-five (25) designated participants (Designated Participants or DPs).¹ Concluding that more information about the DPs was a necessary prerequisite to competently conducting a fair hearing,² I tasked the Government and the DPs with furnishing additional information by November 12, 2024 in an order dated October 31, 2024 (Preliminary Order or Prelim. Ord.). Prelim. Ord. at 3. Most of the DPs timely complied with this directive,³ including the instruction to supply information related to their respective

¹ The American Academy of Hospice and Palliative Medicine withdrew its request to participate in a document filed on November 8, 2024, as did the American College of Occupational and Environmental Medicine on November 12, 2024. Similarly, the National Sheriffs' Association has signaled its intent to submit a hearing waiver. These DPs are no longer parties to this proceeding and no standing recommendations have been made regarding them.

² 5 U.S.C. § 556(c)(5); 21 C.F.R. § 1316.52(c), (g), (h).

³ The International Academy on the Science and Impact of Cannabis (IASIC) and Saint Michael's College (SMC) did not respond to the Preliminary Order. However, Ari Kirshenbaum, PhD is affiliated with SMC, and Kenneth Finn, M.D. is affiliated with IASIC. Neither of these DPs sought to either speak on behalf of these institutions or made any assertions relative to associational standing based on their respective affiliations. IASIC and SMC are no longer parties to this proceeding and this order contains no standing recommendations with respect to them.

arguments for standing under the Administrative Procedure Act (APA) and CSA and its implementing regulations.

The non-legislative transfer of controlled substances from one schedule to another by the DEA⁴ is authorized only “after opportunity for a hearing pursuant to the rulemaking procedures” set forth in the Administrative Procedure Act. 21 U.S.C. § 811(a). Both the Agency’s NPRM and the GNoH expressly invited “interested persons” seeking participation in this potential scheduling action to file applicable requests within specified deadlines. 89 Fed. Reg. at 44598; 89 Fed. Reg. at 70148-79; 21 U.S.C. § 811(a); 21 C.F.R. § 1308.44(a), (b).

The APA provides that “[s]o far as the orderly conduct of public business permits, an interested person may appear before an agency or [one of its ALJs]⁵ for the presentation, adjustment, or determination of an issue, request, or controversy in a proceeding. . . in connection with an agency function.”⁶ 5 U.S.C. § 555(b). When agencies are “charged with administering congressional statutes[, b]oth their power to act and how they are to act is authoritatively prescribed by Congress[.]” *City of Arlington, Tex. v. FCC*, 569 U.S. 290, 297 (2013); see *American Trucking Associations, Inc. v. United States*, 627 F.2d 1313, 1320 (D.C. Cir. 1980) (“When an agency exercises authority expressly delegated to it by Congress it is at the zenith of its powers.”). However, even when operating “at the zenith of its powers,”⁷ the agency is constrained to act within the parameters of the APA, the CSA, and any related regulations, and must refrain from actions which are arbitrary, capricious, and demonstrate an abuse of its Congressionally-authorized discretion. *American Trucking*, 627 F.2d at 1316, 1320-21.

Prior to the commencement of a hearing on the rescheduling of a controlled substance, a threshold determination must be made regarding the proper cadre of hearing participants. Standing to appear in an APA agency proceeding can differ markedly from the rigid standing

⁴ The Attorney General’s CSA authority has been delegated to the DEA Administrator by regulation. 28 C.F.R. § 0.100.

⁵ 5 U.S.C. § 556(b)(3). The APA prescribes only three types of officials that may preside over an agency’s evidentiary hearing: the agency head; one or more members of a body that comprises the agency; or an ALJ appointed in accordance with 5 U.S.C. § 3105. *Id.* at § 556(b). In the Department of Justice, the DEA is organizationally structured to exclusively utilize the third option. The same is true of the Bureau of Alcohol, Tobacco, Firearms, and Explosives (ATF) and the Bureau of Prisons (BOP). Neither the Attorney General nor the DEA Administrator preside over hearings, and neither agency has been equipped by Congress with a body such as the National Labor Relations Board, the Securities and Exchange Commission, or the National Transportation Safety Board to adjudicate factually contested cases.

⁶ It is beyond argument that the scheduling, rescheduling, and descheduling of controlled substances is an agency function assigned to the DEA and specifically authorized by Congress. 21 U.S.C. § 811(a).

⁷ *American Trucking*, 627 F.2d at 1320.

requirements incumbent on those seeking relief in the federal courts. *Fund Democracy, LLC v. SEC*, 278 F.3d 21, 27 (D.C. Cir. 2002) (“Because agencies are not constrained by Article III, they may permit persons to intervene in the agency proceedings who would not have standing to seek judicial review.”). To ensure proper separation of powers from the political branches, Article III, section 2 of the Constitution cabins the jurisdiction of the federal courts to cases and controversies. As such, those appearing before the courts must possess the requisite elements of Article III standing, *to wit*, a demonstration of a particularized injury that is: (1) actual or imminent; (2) caused by, or fairly traceable to an act that the litigant challenges in the litigation; and (3) redressable by the court. *FDA v. Alliance for Hippocratic Medicine*, 602 U.S. 367, 380-81 (2024); *Gettman v. DEA*, 290 F.3d 430, 432-33 (D.C. Cir. 2002). While this Article III standing threshold is present for a party seeking to challenge an action in the courts (even a person challenging an agency action under the APA),⁸ it is not perforce coextensive with the relaxed level of standing required to appear in an agency administrative proceeding. *Gettman*, 290 F.3d at 433-34. The constraints of Article III standing rest “on considerations about the proper—and properly limited—role of the courts in a democratic society,” *Envirocare of Utah, Inc. v. NRC*, 194 F.3d 72, 75 (D.C. Cir. 1999) (quoting *Warth v. Seldin*, 422 U.S. 490, 498 (1975)), whereas federal administrative agencies are not likewise restricted. *See, e.g., New World Radio, Inc. v. FCC*, 294 F.3d 164, 172 (D.C. Cir. 2002); *Envirocare*, 194 F.3d at 74.

A lower standing threshold is often sensible in view of the potential public policy implications of many agency actions, and the application of this less rigorous procedural bar has been recognized, reviewed, and affirmed by the courts. *See, e.g., Gettman*, 290 F.3d at 433-34; *Animal Legal Defense Fund, Inc. v. Vilsack*, 237 F.Supp.3d 15, 21-22 (D.D.C. 2017). Further, as discussed, *supra*, because agencies are not limited in this way by Article III, they may, in their discretion, permit persons to intervene in their proceedings who would not otherwise have standing to seek judicial review of the agency action ultimately taken. *See, e.g., Fund Democracy*, 278 F.3d at 27. However, this is not to say that everyone must be inexorably welcomed to appear before every agency on every issue that touches widely on society or tugs at the heartstrings. The APA limits the ability to appear before an agency to “interested persons,” which Congress further qualified by the phrase “[s]o far as the orderly conduct of public business permits” 5 U.S.C. § 555(b). Regrettably, the legislative histories of the APA and the CSA

⁸ 5 U.S.C. § 702.

are of negligible assistance when narrowing the definition of who properly rests within the parameters of an “interested person” as it pertains to an administrative scheduling hearing before the DEA.

To be sure, agency adjudications (including DEA adjudications) can and do have their own standing requirements that are baked into the process by the APA, their enabling statutes, and their implementing regulations. It follows then, that leave to appear before an agency in its APA adjudications, that is, discernment of who is an “interested person” takes on a different form based on the fixed navigation points, including (and especially) the agency’s regulations.

“[T]he starting point for an APA standing determination for a litigant before an administrative agency is not Article III, but is the statute that confers standing before that agency.” *Ritchie v. Simpson*, 170 F.3d 1092, 1095 (Fed. Cir. 1999). The courts will generally examine an agency’s enabling statute and implementing regulations to discern the intended, reasonable breadth of those with APA standing. *See, e.g., Ritchie*, 170 F.3d at 1095 (The court interpreted the standing language in the Lanham Act more broadly than did the agency.); *Koniag, Inc. v. Andrus*, 580 F.2d 601, 607-88 (D.C. Cir. 1978) (The court held that Alaska Statehood Act’s attendant regulations indicated a broader class of interested parties than had been interpreted by the Secretary of the Interior.). Thus, the proper inquiry is centered around an interpretation of the statute(s) the agency administers. This analysis involves an examination of existing agency precedent, the legislative history of the statute(s), and/or subsequent regulations which the agencies have sought to carve out the proper scope of the relevant statute(s). *Ritchie*, 170 F.3d at 1095.

Turing to the present case, the Supreme Court has characterized the primary objectives of the CSA as aiming “to conquer drug abuse and to control the legitimate and illegitimate traffic in controlled substances” by protecting against the diversion of drugs from legitimate channels. *Gonzales v. Raich*, 545 U.S. 1, 12-13 (2005). Further, the ultimate goal of protecting the public is served by the CSA’s creation of “a comprehensive, closed regulatory regime criminalizing the unauthorized manufacture, distribution, dispensing, and possession of substances in any of the Act’s five schedules.” *Gonzales v. Oregon*, 546 U.S. 243, 250 (2006). In promulgating controls against diversion through the passage of the CSA, Congress manifested its intent to protect the public from the siphoning of dangerous and fungible controlled substances from the “closed regulatory” system. *Id.*

In delimiting the correct scope of public participation in agency proceedings, the courts have acknowledged that agencies possess broad discretion to limit the participation of interested individuals and organizations. *Nichols v. Board of Trustees of the Asbestos Workers Local 24 Pension Plan*, 835 F.2d 881, 897-99 (D.C. Cir. 1987); *Vilsack*, 237 F.Supp.3d at 21-22. Those who qualify as “interested persons” are entitled to participate in the hearing process⁹ so long as their involvement does not compromise the “orderly conduct of public business.” 21 C.F.R. § 1316.52; 5 U.S.C. § 555(b). This right to participate in the hearing process is not “blindly absolute” and considerations regarding the logistics of the hearing must be factored into the conferral of standing.¹⁰ *Easton Utilities*, 424 F.2d at 852. However, in an agency’s exercise of that discretion to limit participation, the courts will not countenance participation denial policies that are unreasonably overbroad or otherwise arbitrary, or merely based on assertions that interventions are generally burdensome or dilatory.¹¹ *Nichols*, 835 F.2d at 897.

Regrettably, the CSA, its legislative history, and its attendant regulations offer little in terms of guidance on the issue of who is an “interested party” in the context of controlled substance scheduling proceedings. The CSA regulations define the term “interested person” as “mean[ing] any person adversely affected or aggrieved by any rule or proposed rule issuable pursuant to [the scheduling provisions set forth in] 21 U.S.C. § 811.” 21 C.F.R. § 1300.01(b); see, e.g., *Schedules of Controlled Substances: Placement of Lorcaserin into Schedule IV*, 78 Fed. Reg. 26701, 26703 (2013). It is noteworthy that, “[t]he phrase ‘person adversely affected or aggrieved’ is a term of art used in many statutes to designate those who have standing to challenge or appeal an agency decision, within the agency or before the courts.” *Dir., Office of Workers’ Comp. Programs, Dep’t of Labor v. Newport News Shipbuilding & Dry Dock*

⁹ The APA intervention right as set forth in 5 U.S.C. § 555(b) “is universally understood to establish” participation rights for interested persons in “on-going agency proceeding[s].” *Block v. SEC*, 50 F.3d 1078, 1085 (D.C. Cir. 1995).

¹⁰ Specifically, the “time of appearance, the status of the proceedings, [and] the administrative avenues established by other statutes and agency rules for participation” should be afforded consideration when fashioning rules of procedure and participation standards in agency proceedings. *Easton Utilities Commission v. Atomic Energy Commission*, 424 F.2d 847, 852 (D.C. Cir. 1970). Further, if the parties participating in an agency proceeding adequately represent the public interest and the interests of the petitioners, limiting the number of parties otherwise entitled to participate may be appropriate to avoid duplicative presentations. See, e.g., *City of San Antonio v. Civil Aeronautics Board*, 374 F.2d 326, 332-333 (D.C. Cir. 1967).

¹¹ A reviewing court’s confidence in an agency’s decision to limit public participation may be further bolstered by an agency’s efforts to adhere to its own rules and procedures as set forth in their governing statutes and implementing regulations. See, e.g., *Easton Utilities*, 424 F.2d at 851 (“We find nothing whatsoever in the record which in any way challenges the reasonableness, the necessity for, or the propriety of this Commission rule. We are confronted only with the Commission’s utilization of this rule under the factual situation of this case.”).

Company, 514 U.S. 122, 126 (1995) (“person adversely affected or aggrieved” interpreted as sufficient to fulfill Article III standing requirements under the APA). By cabining its own scope of the term “interested persons” to include only “person[s] adversely affected or aggrieved by any rule or proposed rule” it is reasonable to conclude that the Agency regulation drafters intended a narrow, somewhat heightened interpretation of those permitted to appear in scheduling actions. 21 C.F.R. § 1300.01(b). There can be little doubt that the stewards of the Agency, at the time the regulation was promulgated, elected to seek input from a potential rules detractors/critics/opponents; in short, those who could demonstrate that they would be “adversely affected or aggrieved”¹² should the proposed rule become law. Stated differently, the Agency was not keen on producing an echo chamber of supportive comments to reinforce its intended result, but focused on hearing from those who feared the consequences of the proposed rule. A restricted standing interpretation is further buttressed by the highly technical nature of the facts to be adduced and analysis employed at a scheduling hearing. 21 U.S.C. § 811(b)-(f). Further, the NPRM, citing 21 C.F.R. § 1308.42, dictates that “the purpose of a hearing would be to receive factual evidence and expert opinion regarding whether marijuana should be transferred to schedule III of the list of controlled substances.” 89 Fed. Reg. at 44599 (cleaned up).

Beyond the stark definition of “interested party”¹³ employed in its regulations, the DEA has not promulgated additional regulations regarding the parameters that could assist in delineating the boundaries of who may appear at its internal proceedings. It is axiomatic that an ALJ may not entertain a challenge to its agency’s regulations,¹⁴ and the DEA has certainly not been bashful about reminding its judges that “[o]nce the [A]gency has ruled on a given matter ... it is not open to reargument by the [ALJ].” *Clair L. Pettinger, M.D.*, 78 Fed. Reg. 61592, 61600 n.13 (2013). Among its published precedential decisions, the Agency has insisted that those seeking APA standing as an “interested person” must, in the hearing request, sufficiently articulate a persuasive basis for their standing. *See, e.g., Schedules of Controlled Substances: Placement of Lorcaserin into Schedule IV*, 78 Fed. Reg. at 26703 (The Agency denied a hearing request filed by a commenter “[b]ecause the commenter failed to provide sufficient information

¹² 21 C.F.R. § 1300.01(b).

¹³ *Id.*

¹⁴ *CropLife America v. EPA*, 329 F.3d 876, 882 (D.C. Cir. 2003); *Iran Air v. Kugelman*, 996 F.2d 1253, 1260 (D.C. Cir. 1993) (“It is commonly recognized that ALJs are entirely subject to the agency on matters of law.”) (internal quotation marks omitted); *Oestereich v. Selective Service System Local Bd. No. 11*, 393 U.S. 233, 242 (1968) (Harlan, J., concurring).

to demonstrate that he meets the definition of “interested person” as set forth in the regulations”).

Relaxed is not synonymous with nonexistent, and an *interesting* person (someone the ALJ—or the Administrator—may subjectively believe possesses the potential for objectively meaningful and insightful input) is likewise not synonymous with an “interested person” (a person entitled to request and participate in an APA hearing before DEA involving the scheduling of controlled substances). The potentially relaxed requirements of APA standing notwithstanding, the Agency has a right to exercise some level of control over those who appear in its proceedings,¹⁵ and a concomitant right to expect its ALJs to adhere to its regulations and its precedents.¹⁶ Contrariwise, that the regulations authorize a narrow segment of the population to *request* and participate in a scheduling hearing (in the case of the CSA regulations, a very narrow segment) does not perforce preclude the Agency (or this tribunal) from hearing and considering viewpoints from those unable to shoulder the burden of establishing standing. Stated differently, the Agency may be at liberty to conclude that its proposed action could benefit somewhat by listening to at least some of those who might support is proposed rule (*i.e.*, the echo chamber). Logically, however, the applicable CSA regulations were clearly drafted in a manner that the views of those participants who demonstrate APA standing (within the bounds of reasonable discretion) should be afforded a stronger voice or more weight in the ultimate decision. A contrary conclusion would arguably eviscerate the purpose for the regulation’s standing standards.

With those parameters in mind, a review of available precedent, in the courts and inside the Agency, reveals some considerations that can inform an equitable determination here on the issue of APA standing in scheduling matters before the DEA.¹⁷ Several of the Agency’s

¹⁵ *City of San Antonio*, 374 F.2d at 329 (“No principle [of] administrative law is more firmly established than that of agency control of its own calendar.”).

¹⁶ *Pettinger*, 78 Fed. Reg. at 61600 n.13.

¹⁷ Agencies, including the DEA, are empowered to issue “interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice” without engaging in the formal notice and comment or hearing procedures set elsewhere in the APA. 5 U.S.C. § 553. It is worth noting, that when presented with the opportunity to adjust its stance on the definition of “interested persons,” the Agency has declined to do so and has demonstrated some level of consistency (albeit sparse in analysis) in fashioning its own view of who is “adversely affected or aggrieved.” See *Consolidation, Elimination, and Clarification of Various Regulations*, 62 Fed. Reg. 13938, 13942 (1997); *Consolidation, Elimination, and Clarification of Various Regulations*, 61 Fed. Reg. 8503, 8508 (1996). In its response to a commenter who sought to amend the definition of “interested person” in proceedings involving the importation of controlled substances, DEA concluded that the definition of “interested person” was “sufficiently

previous scheduling endeavors pursuant to 21 U.S.C. § 811 failed to garner hearing requests,¹⁸ however, there are some analytical navigation points, including measures some other federal agencies have taken (with varying levels of success on review in the courts) to assist in shaping the appropriate contours of APA standing in scheduling actions at DEA. To that end, the issue of whether the DPs have alleged sufficient APA standing to participate in this rescheduling hearing should be assessed by balancing the following four considerations (the Standing Considerations or SCs): (1) whether the requestor possesses a substantial interest in the proceedings (*to wit*, would be adversely affected or aggrieved if the proposed rule were promulgated) and/or otherwise satisfies the requirements of Article III standing; (2) whether the request complies with clear, reasonable procedural agency directives; (3) whether the request exceeds the scope of the NPRM; and (4) whether, in the discretion of the Agency, the participation of a particular requestor would meaningfully assist the decisionmaking and/or whether the interests of multiple requestors are amenable to consolidation or exclusion to accommodate orderly proceedings.

APA Standing Consideration One: Whether the DP/Requestor Possesses a Substantial Interest in the Outcome of the Proceedings (*to wit*, would be adversely affected or aggrieved if the proposed rule were promulgated) **and/or Otherwise Satisfies the Requirements of Article III Standing**. Beyond a doubt, by the plain language of the CSA and its implementing regulations, this is the most powerful and issue-dispositive factor. *Ritchie*, 170 F.3d at 1095; *Koniag*, 580 F.2d at 608. Where a requestor demonstrates a substantial interest in the outcome of an administrative proceeding (*to wit*, aggrievement or adverse affect from promulgation of the NPRM), that requestor should ordinarily have a right to participate. *See BPI v. Atomic Energy Commission*, 502 F.2d 424, 427 (D.C. Cir. 1974). Likewise, a demonstration that a requestor would be entitled, when the adjudication is final, to judicial review of an agency action (*i.e.*, the requestor has proffered enough to satisfy the requirements of Article III standing) will ordinarily

precise to fulfill [its] intended purpose.” *Consolidation, Elimination, and Clarification of Various Regulations*, 62 Fed. Reg. at 13938.

¹⁸ *See, e.g., Schedules of Controlled Substances: Removal of Naloxegol from Control*, 80 Fed. Reg. 3468, 3469 (2015); *Schedules of Controlled Substances: Placement of Brivaracetam into Schedule V*, 82 Fed. Reg. 13067, 13067 (2017); *Schedules of Controlled Substances: Placement of Solriamfetol in Schedule IV*, 85 Fed. Reg. 643, 643 (2020).

qualify that person as an “interested person” who normally should be permitted to be heard in an administrative proceeding. *Nichols*, 835 F.2d at 896; *Vilsack*, 237 F.Supp.3d at 21; *but see Envirocare*, 194 F.3d at 75.¹⁹ *Envirocare* notwithstanding, granting APA standing to a requestor who, in its request and attendant filings, has averred sufficient facts to demonstrate that it would have Article III standing to challenge a DEA scheduling action on appeal in federal court is the analytically superior option. Further, the legislative history of the Controlled Substances Act illuminates that requestors that possess sufficient interest in engaging with the dual goals of the Act (to protect the public’s health and ensure the closed regulatory system of controlled substances) will likely have a strong case for establishing their participation rights.²⁰ In view of the DEA’s narrow definition of “interested person” under its regulations,²¹ this aspect of Standing Consideration One, must generally be afforded controlling weight. That is to say, the Agency’s insistence that some demonstration that the person seeking a ticket to appear in its proceedings articulate a demonstration that the interested person will be “adversely affected or aggrieved by any ... proposed rule,” constitutes a condition precedent for APA standing is not unreasonable. Others who are interested, but do not qualify as “interested persons” under the regulations, may not necessarily be foreclosed from a voice in the process, and had the opportunity to file written comments. 5 U.S.C. § 553(c); 21 C.F.R. § 1308.44(g); 89 Fed. Reg. at 44598. That said, a rational, supported application of the APA qualifier language that interested persons may appear “[s]o far as the orderly conduct of public business permits” can trump standing in APA proceedings. 5 U.S.C. § 555(b); *Vilsack*, 237 F.Supp.3d at 22.

APA Standing Consideration Two: Whether the Request Complies with Clear, Reasonable Procedural Agency Directives. While the Consideration One requirements

¹⁹ The *Envirocare* court relied liberally on *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 84-42 (1984), which has been subsequently reversed by *Loper Bright Enterprises v. Raimondo*, 144 S.Ct. 2244, 2273 (2024).

²⁰ The text and legislative history of the CSA appears bereft of any indication that it was promulgated to protect the employment interests of a registrant. *See, e.g., Bonds v. Tandy*, 457 F.3d 409, 415-16 (5th Cir. 2006) (“a pharmacist’s interest in employment is not arguably within the zone of interests protected by the statute. Accordingly, [the pharmacist] is not a ‘person aggrieved’ under [the CSA]”). *See also, Alliance for Hippocratic Medicine*, 602 U.S. at 385-87 (finding that doctors lacked Article III standing when attempting to challenge the regulation of a drug they did not prescribe or use themselves).

²¹ 21 C.F.R. § 1300.01(b).

are of paramount importance, there are also factors that can potentially further narrow participation, and satisfaction of Consideration One is by no means a *carte blanche* to entry into the proceedings. The courts have upheld an agency's requestor denials based on the failure of the requestor to abide the agency's reasonable procedural requirements. *BPI*, 502 F.2d at 427-29 (Participation denial upheld where requestor failed to fulfill agency requirement to specify the basis for the requested participation.); *Easton Utilities*, 424 F.2d at 850 (Participation denial upheld where requestor submitted petition beyond regulatory deadlines and after hearings had been conducted.). In *Easton Utilities* the court held:

We do not believe that the affirmative grant of a right to appear is blindly absolute, without regard to time of appearance, the status of the proceedings, the administrative avenues established by other statutes and agency rules for participation, or most importantly, as 'the orderly conduct of public business permits.'

424 F.2d at 852. As discussed, *supra*, the DEA currently has no regulations specifically directed towards hearing requestor requirements beyond the bare "interested person" limitation and definition in the CSA and its implementing regulations. Accordingly, resort must be had to the relatively sparse collection of (analytically barren) final orders addressing participation requests, the APA and its interpretive precedent, and the terms of the NPRM. Hearing requests have been rejected by DEA in the face of an individual's failure to comply with procedural directives. See *Placement of Controlled Substances: Placement of Cathinone and 2,5-Dimethoxy-4-ethylamphetamine Into Schedule I*, 58 Fed. Reg. 4316, 4316 (1993) (denying a request for hearing because it was not filed in accordance with the directives as established by the regulation); *Schedules of Controlled Substances: Placement of ()cis-4-methylaminorex into Schedule I*, 54 Fed. Reg. 14799, 14799 (1989) (same). The Agency has held that a requestor must supply some specific information regarding his/her/its theory of standing under the "interested person" standard. See *Schedules of Controlled Substances: Placement of Lacosamide into Schedule V*, 74 Fed. Reg. 23789, 23789 (2009). Similarly, the Agency has interpreted its regulations as requiring that "any person requesting a hearing *must state with particularity* his interest in the proceeding." *Id.* (internal quotations omitted) (emphasis supplied). Inasmuch as the Agency has historically demanded a narrow, individualized,

statement of a requestor's adverse outcome or grievance to merit participation in the scheduling hearing process, the failure to provide one militates against participation.

The NPRM in this case has similarly required that hearing requests in this rescheduling action must: “(1) state with particularity the interest of the person in the proceeding; (2) state with particularity the objections or issues concerning which the person desires to be heard; and (3) state briefly the position of the person regarding the objections or issues.” 89 Fed. Reg. at 44598. In this regard, it is not the place of the ALJ to conduct extra-record research or engage in broad conjecture about the potential benefits of each requestor. These hearing request requirements are not optional, and the evaluation can only be made on the four corners of the Designated Participants' responses to the Preliminary Order (Preliminary Order Responses or PORs).

APA Standing Consideration Three: Whether the Request Exceeds the Scope of the NPRM. Consideration Three presents an additional limitation. As discussed, *supra*, the Agency is authorized to act within the parameters set forth by Congress. In *Olsen v. DEA*, 776 F.2d 267, 267 (11th Cir. 1985), the court upheld a participation denial by members of the Ethiopian Zion Coptic Church (the Church) in pursuit the Church's efforts to acquire a religious exemption for its members to use marijuana. The Church petitioned for rescheduling under 21 U.S.C. § 811, and the court held that an effort to seek a religious exemption fell outside the (scheduling) scope of § 811. *Id.* Thus, a requestor who seeks participation to acquire relief that is outside the scope of rescheduling (*e.g.*, descheduling, decriminalization, etc.) can properly be denied on that basis alone.

APA Standing Consideration Four: Whether, in the Discretion of the Agency, the Participation of a Particular Requestor Would Meaningfully Assist the Decisionmaking and/or Whether the Interests of Multiple Requestors are Amenable to Consolidation or Exclusion to Accommodate Orderly Proceedings. The DEA Administrator has been charged by Congress in exercising discretion in assigning schedule placement for a plethora of potentially dangerous, addictive medications. 28 C.F.R. § 0.100; 21 U.S.C. § 811. It is imperative that she and her Agency possess the latitude to regulate participation

to include requestors who can render meaningful assistance to her determination, and to exclude those who are not objectively in a position to do so. *Cf., Nichols*, 835 F.2d at 897 (agencies should have discretion to exclude requestors who would fail to assist the agency's decisionmaking); *Cities of Statesville v. Atomic Energy Commission*, 441 F.2d 962, 977 (D.C. Cir. 1969) (agencies should have broad discretion to determine the sources reasonably required to supply the assistance it needs in vindicating the public interest). Thus, if there is a requestor who possesses information that the DEA Administrator deems keenly important to rendering a scheduling determination that is legally correct and consistent with public interest within the meaning of the CSA, she must be afforded a healthy level of discretion to grant participation. This Consideration by no means creates APA standing, but on a pragmatic level, the Administrator, through her Government counsel, are permitted to call witnesses at a contested hearing, and her inclination to hear from a wider spectrum of society is entitled to a level of deference.

Reasonable, pragmatic considerations on the part of the agency are also valid. Even parties with a solid, substantial interest in the proceedings (Consideration One) are not immune from logistical concerns. In upholding the authority of an agency to limit and consolidate an unwieldy number of requestors, the D.C. Circuit rendered the following holding:

Practical problems of calendar administration confront an agency whenever related applications are pending at the same time. Consolidation, scope of the inquiry, and similar questions are housekeeping details addressed to the discretion of the agency and, due process or statutory considerations aside, are no concern of the courts.

City of San Antonio, 374 F.2d at 329. An agency may take reasonable steps to avoid obstructing or overburdening the proceedings, or to avoid unduly broadening the issues considered. *Nichols*, 835 F.2d at 897. Thus, the DEA is not required to accommodate a cast of thousands in conducting its scheduling hearings, and may, where appropriate, prescribe reasonable limits based on size and common interests of the requestors.²² As

²² The court went on to explain in *City of San Antonio* that while true “that a party with a substantial interest in the proceeding has a right to intervene . . . But a finding of substantial interest must be related to a particular proceeding. And a proceeding must be manageable if it is going to be conducted in such a manner as will be conducive to the proper dispatch of business and to the ends of justice.” *Id.* at 332 (internal citation and punctuation omitted); *see also, Cities of Statesville*, 441 F.2d at 977 (*en banc*) (Even in the face of a substantial interest on the part of a requestor “an agency should be accorded broad discretion in establishing and applying rules for public participation,

discussed, *supra*, the APA qualifies the appearance rights of participants with the language “[s]o far as the orderly conduct of business permits,”²³ so long as the discretion is exercised rationally. *Vilsack*, 237 F.Supp.3d at 24. As a result, the consolidation of parties may be a necessary function of the administrative hearing process. When resolving procedural issues, such as consolidation, that are not specifically addressed by the relevant authorities (the APA, the CSA, and their implementing regulations), the Federal Rules of Civil Procedure provide useful guidance.²⁴ Rule 42(a) of the Federal Rules of Civil Procedure authorizes the consolidation of actions that “involve a common question of law or fact” by permitting the judge to “join for hearing . . . any or all matters at issue in the actions;” “consolidate the actions; or” “issue any other orders to avoid unnecessary cost or delay.” The trial judge²⁵ is afforded “large discretion in the matter [of consolidation] which will not be interfered with except in a clear case of abuse” *Davis v. Yellow Cab Co.*, 220 F.2d 790, 791 (5th Cir. 1955). There is no magic quantum of common facts (or law) and likewise no disparity as to which party’s evidence should weigh in (or be omitted from) the analysis. Under the like considerations that support case consolidation, when requestors present overlapping or duplicative interests and proposed testimony, this may pose a powerful and persuasive reason to “avoid unnecessary cost or delay” through either limitation of viewpoints, or even consolidation of parties. Fed. R. Civ. P. 42(a). “Participation in agency [APA rulemaking] proceedings does not necessarily entail full-fledged party intervention. Rather, agencies have ample authority to shape the manner in which intervenors will participate.” *Vilsack*, 237 F.Supp.3d at 24 (quotation marks and internal citation omitted).

As discussed, *supra*, this tribunal has not been furnished with copies of the responses filed by the DPs with the Administrator. Accordingly, the APA standing determinations set forth

including how many are reasonably required to give the agency the assistance it needs in vindicating the public interest”) (internal punctuation and quotation marks omitted).

²³ 5 U.S.C. § 555(b).

²⁴ *But see*, *Roy E. Berkowitz, M.D.*, 74 Fed. Reg. 36758, 36759 (2009) (noting that DEA administrative hearings are not bound by the Federal Rules of Civil Procedure); *Kamir Garcés-Mejías, M.D.*, 72 Fed. Reg. 54931, 54932 (2007) (same).

²⁵ The Supreme Court, in reviewing the boundaries of immunity relative to an agency ALJ, has held that “[t]here can be little doubt that the role of the modern federal . . . administrative law judge within [the framework of the APA] is ‘functionally comparable’ to that of a [U.S. District Court] judge.” *Butz v. Economou*, 438 U.S. 478, 513 (1978). While the scope of this functional equivalence is not without limitations, it is correctly applied to the issuance of procedural rulings within the context of an APA administrative hearing.

herein are rendered based exclusively on an evaluation of the Preliminary Order Responses provided by the Designated Participants. The respective determinations have been made light of the Four APA Standing Considerations (SCs One-Four) discussed above, and (in no particular order) will be herein evaluated *in seriatim*.

Cannabis Bioscience International Holdings (CBIH)

In its POR, CBIH describes itself as “a corporation devoted to research and development in healthcare, particularly in cannabinoid-based formulations aimed at advancing medical treatment options for serious diseases.” CBIH POR at 1. This requestor elaborates that its “mission centers on leveraging the therapeutic potential of cannabis-derived compounds to enhance patient care and broaden the scientific understanding of cannabis in medical applications.” *Id.*

As its basis for APA standing, CBIH represents that it anticipates that the placement of marijuana in Schedule III will “facilitate significant advancements in medical research, patient care, and regulatory clarity, directly impacting [CBIH’s] ability to conduct cannabinoid-based research” and that the proposed rescheduling would be “integral to CBIH’s mission to provide safe, accessible, and evidence-based cannabis-derived treatments, which would be otherwise constrained under the existing Schedule I classification.” *Id.* at 2. Further, CBIH represents that rescheduling would advance its intellectual property goals, and specifically catalogues a list of recently-filed patent applications. *Id.*

The POR regarding this requestor does not specify how it would be “adversely affected or aggrieved” by the *promulgation* of the proposed rescheduling rule, but rather, explains that its research and pecuniary interests would be advanced by rescheduling. This is a requestor who aspires to pursue the purported benefits of marijuana for commercial use. Thus, this requestor has not demonstrated that it would be adversely affected or aggrieved by promulgation of the NPRM, and instead avers that it will not accrue the benefits it aspires to in the event marijuana is not rescheduled into Schedule III. Rescheduling presents a potential benefit to this requestor, but declining to do so will not adversely affect its interests beyond the status quo. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor’s benefit.

Under SC Two (compliance with procedural directives), the RFH was apparently timely, and the POR is clear in its support of the proposed rescheduling, discusses the issues upon which it desires to be heard, and adequately outlines its position. On the whole, this requestor has complied with the relevant Preliminary Order and the procedural directives of the Agency in the NPRM. Thus, SC Two does not disfavor APA standing.

Similarly, inasmuch as the POR is laser focused on the rescheduling depicted in the NPRM and its potential impact on CBIH, SC Three (within the scope of the NPRM) militates in favor a grant of APA standing for this requestor.

Regarding SC Four (Meaningful Assistance/Consolidation Potential), a company dedicated to developing new, medically significant formulations of marijuana products with shared scientific and commercial objectives could potentially have expertise and access to relevant information that could potentially be helpful to the Agency in deciding whether to proceed with its proposed rescheduling rule. Beyond that, the Administrator has identified this requestor as a DP, which is entitled to significant deference. Inasmuch as CBIH shares a pecuniary/commercial concern with other requestors, it may be prudent to consider a consolidation of presentations with other DPs who also favor the proposed rescheduling.

Upon a thoughtful balance of the four SC Factors, CBIH has certainly not demonstrated that promulgation of the NPRM will adversely affect or aggrieve its interests within the unambiguous, directive terms of the regulations. Upon consideration of the powerful Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Analyzing the other SC Factors (in particular, SC Four, as evidenced by the Administrator's designation) militate in favor of CBIH's participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision.

International Association of Chiefs of Police (IACP)

In its POR, the IACP describes itself as "the world's largest and most influential professional association for police leaders ... committed to advancing safer communities through thoughtful, progressive police leadership." IACP POR at 1. This requestor claims to "speak[] out on behalf of law enforcement." *Id.*

IACP's POR opposes the NPRM because, in its view, the proposed rescheduling change would present "a significant shift in federal drug policy with significant implications for public safety, public health and the ability of police agencies to protect the public," presumably all of which would negatively impact on, *inter alia*: policing, firearms regulations, public and workplace safety, impaired driving, impairment standards, and firearms regulation. *Id.* at 2.

In this regard, IACP's assertion of standing under SC One (aggrievement, adverse impact or Article III standing) depends entirely upon its ability to demonstrate associational standing.

An association only has standing to bring suit on behalf of its members when its members would otherwise have standing to sue in their own right, the interests [the association] seeks to protect are germane to the organization's purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit.

Fund Democracy, 278 F.3d at 25 (citing *Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.*, 528 U.S. 167, 181 (2000)). Here, the interests cited by IACP, at least as articulated as adverse (that is, the potentially adverse impact rescheduling could have on the law enforcement efforts to enforce driving and other impairment-related and fit-for-duty laws regularly enforced by many of its members), could conceivably be adversely impacted by promulgation of the NPRM. Accordingly, SC One favors standing in this case.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential), the POR posits a wide reservoir of access to members with the potential to speak authoritatively on the listed issues of concern, a law enforcement perspective is quite valuable, and even beyond all that, that the Administrator approved IACP's status as a DP is entitled to significant deference. The law enforcement focus expressed by this requestor may well be best served by consideration of consolidation with other like-minded requestors.

Accordingly, inasmuch as all four of the SCs favor standing, this DP has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor may wish to give serious consideration to presentation consolidation with other enforcement-motivated requestors who are unsupportive of the proposed rescheduling.

Veterans Initiative 22 (VI-22)

In its POR, VI-22 defines itself as “a non-profit organization whose mission is veteran suicide prevention” and that its focus is helping veterans, their families and first responders “by providing resources, employment opportunities, and ... advocating for safe access to affordable cannabis” VI-22 POR at 2. The POR does not reference any specific or estimated number of veteran members or beneficiaries or how its services are designed to assist those veterans, but it does posit that the NPRM would facilitate cannabis research, improve veterans’ access to marijuana as an alternative treatment option, and reduce legal barriers to veterans who seek to use marijuana as medicine. *Id.* at 5.

It is not necessary to reach the issue of associational standing. Irrespective of the size of its membership or the scope of its beneficiaries, VI-22’s POR does not specify how it or its beneficiaries would be “adversely affected or aggrieved” by the *promulgation* of the proposed rescheduling rule. It is VI-22’s stated position that those it helps would markedly benefit by DEA’s embracement of the NPRM and rescheduling of marijuana to Schedule III. Specifically, the POR argues that promulgation of the NPRM will encourage research into the substance’s benefits, make it more accessible to veterans, and diminish some legal barriers that affect the organization’s beneficiaries. Thus, this requestor has not demonstrated that it or those it assists would be adversely affected or aggrieved by promulgation of the NPRM. Rescheduling presents a potential benefit to this requestor and its veterans, and will not adversely affect any of its espoused causes related to marijuana. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor’s benefit.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). The POR’s demonstration under SC Four (Meaningful Assistance/Consolidation Potential) is stronger on its commitment to its positions than it is on access to a wide range of relevant experts, but that the Administrator approved VI-22’s status as a DP is entitled to significant deference.

Upon a thoughtful balance of the four SC Factors, VI-22 has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve its own interests or the interests of those on whose behalf it advocates. Placing appropriate regulatory emphasis on the powerful

Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Consideration of the other SC Factors (in particular, SC Four, as evidenced by the Administrator’s designation) lend some support to allowing this requestor’s participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision. The veteran-focused concerns of this requestor may lend itself well to consolidating its presentation with other veteran-focused DPs who also favor promulgation of the NPRM.

Kenneth Finn, M.D.

Dr. Finn’s POR lists his extensive medical qualifications and his considerable experience writing, lecturing, and testifying on the issue of marijuana use. Finn POR at 1. Although affiliated with numerous organizations, including the International Academy on the Science and Impact of Cannabis,²⁶ the POR identifies his interest in the NPRM exclusively as a physician, and not on behalf of IASIC or any other organization, thereby precluding consideration of associational standing. According to the POR, this requestor has multiple relevant board certifications and practices pain medicine. *Id.* Dr. Finn alleges that as a physician, the promulgation of the NPRM would adversely affect him because the lack of satisfactory research into cannabis and the absence of any dosing guidelines or care standards from the Food and Drug Administration (FDA) would render him unable to competently prescribe or administer the substance as a drug for his patients. *Id.* at 1-3.

In *FDA v. Alliance for Hippocratic Medicine*, the Supreme Court held that a group of physicians challenging FDA regulations lacked standing to do so based on anticipated hurdles in patient treatment. 602 U.S. at 380-81. The Court specifically declined to create a “doctor standing” doctrine,²⁷ but was equally unambiguous in holding that the plaintiff-doctors “may present their concerns and objections to the President and FDA in the regulatory process” *Id.* at 397. Which segues nicely to the subject of APA standing. As discussed, *supra*, the requirements of APA standing are not coextensive with standing under Article III, and are principally driven by the applicable agency regulations. *Ritchie*, 170 F.3d at 1095. Here, Dr.

²⁶ *Supra* note 3.

²⁷ *Id.* at 391-92.

Finn has raised issues related to his pain management practice where he claims that he will be adversely affected by the promulgation of the NPRM. Without reaching the issue as to whether any of his anticipated difficulties have merit, this type of allegation clearly sounds within the reach of the APA and CSA's standing requirements under the regulations, and militate in favor of standing under SC One (aggrievement, adverse impact or Article III standing).

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential), the POR essentially offers the potential testimony of Dr. Finn, whose credentials arguably represent a considerable array of subject matter experience and knowledge on subjects relevant to the NPRM determination. Furthermore, the Administrator approval of Dr. Finn's status as a DP is entitled to significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, this DP has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. The medical practitioner-focused interests of this requestor may render it sensible for him to consider presentation consolidation with other, medical practitioner DPs who also disfavor the proposed rescheduling action.

Phillip Drum, PharmD

Dr. Drum's POR lists his extensive qualifications as a pharmacist and his considerable experience writing, lecturing, and testifying on the issue of marijuana use and impairment. Drum POR at 1-2. Dr. Drum alleges that as a pharmacist, the promulgation of the NPRM would adversely affect him because, at least in his view, the FDA did not perform the functions that pharmacists depend upon for the safe, effective, and professional exercise of pharmacy. *Id.* Specifically, the lack of the package inserts required to accompany all medications will, at least in his view, result in an inability to comply with the standards of his profession. *Id.* According to Dr. Drum's POR:

As a [Schedule III] product, marijuana products need an approved package insert listing medical indication for use, scientific evidence of the benefits exceeding the risks, use in the approved indication, the appropriate dosage for various patient populations (age, pregnancy status, metabolic and clearance status, etc.), potential

adverse effects along with the incidence of occurrence, standard concentrations of active ingredients (there are over 100+ cannabinoids in marijuana), storage requirements and clinically relevant drug interactions. Dispensing these products without such information pose[s] a safety risk and inability of a pharmacist to provide required patient education about the safe use of their medicine. None of this information for marijuana has been performed [sic] by the FDA, unlike the package insert currently available for the single [sic] cannabinoid products – dronabinol and cannabidiol.

Id. at 1-2. Thus, by Dr. Drum's reckoning, without research and action by FDA, he cannot do his job and serve his pharmacy patients within the standards of his profession.

As discussed, *supra*, inasmuch as in *Alliance for Hippocratic Medicine*, the Supreme Court declined to create standing for physicians, it is beyond doubt that a similar logic precludes Article III standing for Dr. Drum based exclusively on his status as a pharmacist. 602 U.S. at 396. As has been discussed extensively, elsewhere in this order, the requirements of APA standing are not coextensive with standing under Article III, and are principally driven by the applicable agency regulations. *Ritchie*, 170 F.3d at 1095. Here, Dr. Drum has raised issues related to pharmacy practice, and claims that he and his patients stand to be adversely affected by the promulgation of the NPRM. Without reaching the issue as to whether any of his anticipated difficulties have merit, this type of allegation clearly sounds within the reach of APA/CSA standing under the regulations, and militate in favor of standing under SC One (aggrievement, adverse impact or Article III standing).

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential), Dr. Drum's POR exclusively offers his own potential testimony, which arguably appears to reflect a considerable breadth of subject matter experience and knowledge on subjects relevant to the NPRM determination. Furthermore, the Administrator approval of Dr. Drum's status as DP's is entitled to significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, this DP has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS.** The medical practitioner-focused interests of this requestor may render it

sensible to consider presentation consolidation with other, medical-practitioner DPs who also disfavor the NPRM.

Community Anti-Drug Coalitions of America (CADCA)

CADCA's POR states that it represents "over 7,000 substance use prevention coalitions that involve multiple sectors of a community including schools, law enforcement, youth, parents, healthcare, media, tribal communities and others who are involved in comprehensively addressing locally identified substance use issues, including marijuana." CADCA POR at 2. According to this DP, the mission of its members "is to keep communities safe, healthy and drug free by stopping, delaying and mitigating initiation into substance use" *Id.* CADCA asserts that promulgation of NPRM would greatly increase funding sources of pro-marijuana entities, and thereby render it more difficult to achieve mission goals within its budget, thereby greatly reducing the support it will be able to render to its coalition members. *Id.* at 6.

SC One (aggrievement, adverse impact or Article III standing) consideration is dependent upon a determination that CADCA has associational standing. That is, that CADCA's "members would otherwise have standing to sue in their own right, the interests [the association] seeks to protect are germane to the organization's purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *Fund Democracy*, 278 F.3d at 25 (citing *Friends of the Earth*, 528 U.S. at 181). Assuming (as proffered) that its substance abuse coalitions are uniformly dedicated to the local and national reduction of marijuana use, each one would be adversely affected by a regulatory action that would potentially disproportionately fund pro-marijuana advertising and advocacy efforts. Accordingly, CADCA has demonstrated sufficient associational standing to have that factor militate in favor of standing under SC One.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four, as described in the POR, CADCA's seven-thousand-member-coalition breadth would apparently make a potentially large number of experts with knowledge available to contribute to potentially add meaningful

input to the Agency's NPRM determination. Furthermore, that the Administrator approved CADCA's status as a DP is entitled to significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, CADCA has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. The substance-abuse-prevention focus of this requestor may be best served by considering consolidation of its presentation with other abuse-prevention-motivated DPs who also are unsupportive of the proposed rescheduling.

Cannabis Industry Victims Educating Litigators (CIVEL)

In its POR, CIVEL describes itself as “a marijuana industry victims’ advocacy organization” and alleges that its “victims of the marijuana industry ... have been, are being, or will actually be harmed by [promulgation of the NPRM because it] will increase the use of marijuana, reduce the perception of its dangerousness and lower medical standards for deciding what is a medicine”²⁸ CIVEL POR at 4. While not altogether clear from the POR, CIVEL is apparently engaged in the active representation of individuals who claim/have claimed harmful effects from marijuana, and equips trial attorneys and the public with legal citations and tactical approaches for engaging in anti-marijuana litigation. *Id.* at 3-4.

Reviewing its POR under SC One (aggrievement, adverse impact or Article III standing) CIVEL's APA standing is dependent on whether it has made a persuasive case for associational standing. That is, that CIVEL's “victims” “would otherwise have standing to sue in their own right, the interests [the association] seeks to protect are germane to the organization's purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit.” *Fund Democracy*, 278 F.3d at 25 (citing *Friends of the Earth*, 528 U.S. at 181). Assuming (as proffered) that the “victims” it advocates and litigates for allege they have each been harmed by marijuana and an NPRM that could potentially increase its societal prevalence exponentially, each of the “victims” could allege sufficient harm to justify

²⁸ The POR purports to contain citations for two cases where state courts have granted associational standing for CIVEL under state law. CIVEL POR at 4. While a limited, excerpted portion of an unreported New York trial court decision that was supplied by CIVEL appears to find associational standing by placing reliance on an affidavit executed by one of the plaintiffs (*Cannabis Impact Prevention Coalition and Cannabis Industry Victims Seeking Justice, et al v. Hochul, et al*, Albany County, NY, Index No. 905386-23), the other case (*Botteon and CIVEL, et. al., MID-L-001241-24*) is arguably less helpful in this regard.

associational standing for this DP. Accordingly, CIVEL has demonstrated sufficient associational standing to have that factor militate in favor of standing under SC One.

Regarding SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four, as described in the POR, CIVIL's active litigation and litigation support missions provide a sufficient basis to conclude that it would possess knowledge that could be instrumental in an accurate disposition of this NPRM determination. Furthermore, that the Administrator approved CIVEL's status as a DP is entitled to significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, CIVEL has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. The substance-abuse-prevention/victim focus of this requestor may be best served by considering consolidation of its presentation with other, abuse/prevention requestors who also oppose the NPRM.

Hemp for Victory (HFV)

In its POR, HFV defines itself as "a non-profit organization dedicated to educating the public about why veterans are using medical cannabis over prescription pharmaceuticals, including dangerous and addictive opioids and other controlled substances." HFV POR at 1. The POR explains the organization's mission as "educat[ing] and bring[ing] awareness to the natural solution of cannabis as a way for veterans to manage the mental and physical challenges that often result from military service and to ensure that veterans face neither discrimination nor penalty for their use of medical marijuana." *Id.* The POR does not reference any specific or estimated number of veteran members or beneficiaries, but outlines its education and advocacy mission, and asserts that:

Because of marijuana's [S]chedule I status under federal law, [HFV's] veteran [b]oard members and the veterans for whom they advocate currently face both discrimination and liability if they use medical marijuana. As a result, they cannot obtain access to medicine that they need from the Department of Veterans Affairs and are, in many cases, forced to rely instead on the harmful pharmaceutical drugs that are driving much of our veteran suicide epidemic.

Id. at 4.

It is not necessary to reach the issue of associational standing here. Irrespective of the size of its membership or the sincerity of the organization's commitment, HFV's POR does not specify how it or its beneficiaries would be "adversely affected or aggrieved" by the *promulgation* of the proposed rescheduling rule. HFV's POR is not shy about stating that its goal is the descheduling of marijuana altogether (not part of this NPRM in any way). However, it is HFV's stated position that the placement of cannabis into Schedule III would present "an incremental step toward its ultimate goal" of removing marijuana from the list of scheduled drugs entirely. *Id.* at 5. Thus, this requestor has not demonstrated that it or those it advocates on behalf of would be adversely affected or aggrieved by promulgation of the NPRM. Actually, as conceded by its POR, rescheduling presents a potential benefit to this requestor and its veterans, and will not adversely affect any of its espoused educational and advocacy causes related to marijuana. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor's benefit.²⁹

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is generally within the proper scope of the NPRM (SC Three). The POR's demonstration under SC Four (Meaningful Assistance/Consolidation Potential) names a single witness, but that witness certainly presents as a potential source of authoritative information that could prove helpful in the decision the Agency must make. Additionally, the Administrator's approval of HFV as a DP warrants significant deference.

Upon a thoughtful balance of the four SC Factors, HFV has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve its own interests or the interests of those on whose behalf it advocates. Placing appropriate weight on Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN**

²⁹ The balance of this requestor's arguments in favor of standing are wholly unpersuasive. To argue, at this procedural juncture, that the DEA is an improper advocate or sponsor of its own NPRM adds nothing to the standing equation and (at least on the present record) presents little more than an *ad hominem* distraction from the important advocacy and adjudicative work to be accomplished in these proceedings. A separate motion has been filed on this issue and it will be addressed in a separate order. Further, that HFV has been accorded associational standing in unrelated proceedings where a member had the ability to demonstrate Article III standing does not advance its argument in these proceedings regarding its APA standing.

THESE PROCEEDINGS. Consideration of the other SC Factors (in particular, SC Four, as evidenced by the Administrator’s designation) lend some support to allowing this requestor’s participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision. This requestor remains a DP, and may be well served by considering a consolidation of presentation with other veteran-access-focused participants who also favor the proposed rescheduling action.

National Drug & Alcohol Screening Association (NDASA)

In its POR, NDASA identifies itself as “a non-profit professional association representing more than 5,000 private and public sector employers and service agents, domestically and internationally, who administer and manage workplace drug and alcohol testing programs.” NDASA POR at 1. Drug testing by NDASA members is carried on in the private and public sectors and regulated by various government standards. In addition to a high level of private-sector testing, the government testing includes the Nuclear Regulatory Commission (NRC) and the U.S. Department of Transportation (DOT). *Id.* at 1-2. The DOT testing is carried out in accordance with mandatory statutory and regulatory requirements. Because, according to NDASA, the authority of the U.S. Department of Health and Human Services (HHS) to test only extends to controlled substances in Schedules I and II (not III), promulgation of the NPRM would cause a cessation of marijuana drug testing in key transportation safety positions, to include the following: “airline pilots, air traffic controllers, school bus drivers, subway and train operators, ferry operators, pipeline operators, and truck drivers.” *Id.* at 3. At least in the view of the requestor, this feature of the NPRM would cause its membership to suffer profound and detrimental financial and professional consequences. For these reasons, and reasons of public safety, NDASA opposes the NPRM.

As its POR is structured, standing under SC One (aggrievement, adverse impact or Article III standing) is dependent upon a determination that NDASA has associational standing. That is, that NDASA’s “members would otherwise have standing to sue in their own right, the interests [the association] seeks to protect are germane to the organization’s purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit.” *Fund Democracy*, 278 F.3d at 25 (citing *Friends of the Earth*, 528 U.S. at 181). Assuming (as proffered) that rescheduling marijuana to Schedule III would inflict financial and

professional harm on its members, NDASA has demonstrated sufficient associational standing to have this critical factor militate in favor of standing under SC One.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential) NDASA's POR references the organization's executive director, but in view of the size and specialization of this requestor, it would seem that it would have no shortage of qualified witnesses among its five-thousand-strong membership that could prove helpful in the decision the Agency must make. Additionally, the Administrator's approval of NDASA as a DP warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, NDASA has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor could potentially benefit by considering consolidation with another requestor whose focus is founded in concerns over the potential limitations the NPRM may inflict upon testing for public safety.

The Commonwealth Project (TCP)

In its POR, TCP defines itself as an entity "committed to advocating on behalf of and prioritizing the 65+ population and integrating medical cannabis into mainstream health care for seniors." TCP POR at 1. This requestor appears to be an advocacy group focused on senior citizens and claims to be "rooted in the belief that medical cannabis could be harnessed to not only provide older Americans with an alternative to traditional prescription medications, including opioids, but to reduce soaring health care costs saddling millions of seniors." *Id.* at 2.

On the issue of SC One (aggrievement, adverse impact or Article III standing), the POR's description of TCP renders it unnecessary to reach the issue of associational standing. The POR does not specify how it or its senior-beneficiaries would be "adversely affected or aggrieved" by the *promulgation* of the proposed rescheduling rule. In fact, according to its POR, the only potential aggrievement to this requestor and those seniors it advocates for would be "if rescheduling is rejected or unduly delayed." *Id.* at 3. Not only would the proposed rescheduling not adversely affect or aggrieve this organization, but it has posited that it cannot happen fast

enough for its liking. Accordingly, consideration of SC One does not inure to this requestor's benefit.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR (while perhaps not altogether clear as to how the requestor executes its objectives) is generally responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is within the scope of the NPRM (SC Three). The POR's demonstration under SC Four (Meaningful Assistance/Consolidation Potential) does not identify a particular witness or source of expertise that would be particularly knowledgeable, but a source of the perspective of senior citizens added to the decisional equation would be important and potentially helpful to a resolution of the NPRM. Additionally, the Administrator's approval of TCP as a DP warrants significant deference.

Upon a thoughtful balance of the four SC Factors, TCP has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve its own interests or the interests of those on whose behalf it advocates (just the opposite in fact). Placing appropriate weight on Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Consideration of the other SC Factors (in particular, SC Four, as evidenced by the Administrator's designation) lend some support to allowing this requestor's participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision. This requestor's access-for-seniors focus may be enhanced by consideration of presentation consolidation with other requestors focused on seeking marijuana access for specific groups (*e.g.*, veterans).

The National Transportation Safety Board (NTSB)

The POR filed by the NTSB provides the following account of its background, status, and mission:

The NTSB is an independent federal agency charged by Congress with investigating every civil aviation accident in the United States and significant events in the other modes of transportation—railroad, transit, highway, marine, pipeline, and commercial space.

NTSB POR at 1. According to NTSB, under current law, rescheduling marijuana to Schedule III would place it outside the parameters of authorized drug testing, “prevent[ing] testing for marijuana use by safety-sensitive employees in commercial transportation operations, such as truck drivers, rail conductors, pipeline/hazardous materials operators, air traffic controllers, flight attendants, and airline pilots, among many others.” *Id.* at 2. In NTSB’s view, this result would “create a safety blind spot that could endanger the public, contrary to NTSB’s public safety mission.” *Id.* at 3. NTSB’s POR expresses additional concerns related to the effect of increasing marijuana use in public, due to what it characterizes as “performance-impairing effects” on humans who operate by, with, and in the public transportation sphere. *Id.*

Inasmuch as its representations depict the potential for (in its view) a profound impact on its mission and its ability to safeguard the public in the transportation space, this requestor has established standing under Article III, and its position militates strongly in favor of standing under SC One (aggrievement, adverse impact or Article III standing).

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is squarely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential) as the lead agency in evaluating major traffic incidents and the relevance and extent of any attendant impairment issues, it is likely that this requestor has access to experts in the field that could meaningfully assist in the adjudication of this NPRM. Additionally, the Administrator's approval of NTSB as a DP warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, NTSB has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor could potentially benefit by considering consolidation with another requestor whose focus is concerns over the potential limitations the NPRM may inflict upon testing for public safety.

The Doc App, Inc., d/b/a My Florida Green (DocApp)

In its POR, DocApp describes itself as “a company that supports over 43,000 medical marijuana patients in Florida [which] provides a HIPAA-compliant platform offering real-time analytics, data-driven insights, and treatment support for marijuana patients.” DocApp POR at 2.

Even a cursory reading of this Designated Participant's POR reveals that the DocApp's primary interest in these proceedings' rests solely on the utilization of its platform in future actions involving the possible rescheduling of marijuana to Schedule III. To be sure, input into the process is only enhanced by entities with a potential commercial perspective in the proposed rescheduling action. Here, however, in place of expressing a position on the NPRM, the POR characterizes the NPRM as a "positive step," and emphasizes that it is essential that marijuana patients maintain "flexibility to select what best meets their needs, guided by real-time data on strain options, effects, and availability." *Id.* at 3. This emphasis stands in some tension with the CSA's implementing regulations, which unambiguously provide that "[t]he responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription." 21 C.F.R. § 1306.04(a). Furthermore, the Supreme Court has made clear that medical standards are a function of a state's police powers, not the DEA. *Gonzales*, 546 U.S. at 274. Patient control (as contrasted with input to his/her prescriber/pharmacist) is inconsistent with the regulatory dynamic of prescribing controlled substances, and setting a federal standard for the dispensing and prescribing of controlled substances is well beyond the CSA's statutory mandate. *Id.* at 272, 274-75.

A reading of this DP's POR reflects, at best, mild positivity regarding the NPRM and does not indicate any manner in which it, its customers, or its business interests would be even marginally affected by the proposed rescheduling. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor's benefit in any perceivable way.

Under SC Two (compliance with procedural directives), the RFH was apparently timely, and POR provided identifying and mission information. Beyond that, this DP did not comply with the DEA Administrator's directives to state with particularity its interest in the proceeding, state with particularity the objections or issues concerning which it desires to be heard, and state its position regarding objections or issues. 89 Fed. Reg. at 70149. Likewise although responding to the Preliminary Order, the POR did not state "why/how the DP would be sufficiently 'adversely affected or aggrieved' by the proposed scheduling action to qualify as an 'interested person' under the regulations." Prelim. Ord. at 3. Thus, SC Two does not militate in favor of APA standing.

With respect to SC Three (within the scope of the NPRM), as discussed, *supra*, inasmuch as this POR seeks relief that is beyond the NPRM (*to wit*, the adoption of regulations focused on the inclusion of its software or something like it), and even beyond the regulations and the proper scope of the CSA as determined by the Supreme Court, consideration of this factor does not at all support APA Standing.

Regarding SC Four (Meaningful Assistance/Consolidation Potential), as also discussed, *supra*, input from commercial interests are a proper and valuable area of consideration in deciding whether to reschedule marijuana or any other drug, but this DP is not raising a single issue that could or should be addressed by the NPRM. To be sure, the Administrator has identified this requestor as a DP, but the POR filed is so bereft of any demonstration of standing (or even relevance) has **NOT DEMONSTRATED STANDING AND MAY NOT INDEPENDENTLY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor should expeditiously consider potential consolidation with another, similarly aligned, commercially-motivated requestor. The Administrator's designation is an essential element to be afforded (as evident in the balance of this order) to powerful (and generally controlling) deference regarding participation. But the Administrator did not have the benefit of the POR filed by this DP, and deserves, at a minimum, the analysis offered here. To be clear, based on the content of its POR, this DP has not demonstrated a sufficient (standing or evidentiary) basis to participate in this hearing in the absence of sponsorship by or consolidation with a DP who has demonstrated at least sufficient grounds to be heard.

The State of Nebraska (Nebraska)

In its POR, pertinent to SC One (aggrievement, adverse impact or Article III standing) Nebraska asserts that because under state law, marijuana is "illegal in all circumstances," rescheduling to Schedule III will "supercharge the marijuana industry" and "will increase the many costs and expenditures by Nebraska's law enforcement agencies, its judiciary, and its penal system directly related to or arising from marijuana industry." Neb. POR at 1-2. Inasmuch as its representations depict the potential for pecuniary costs and (in its view) public safety challenges,

this requestor has established standing under Article III, and this militates strongly in favor of standing under SC One.³⁰

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is entirely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential) it is self-evident that the official view of a state regarding the impact of the NPRM on its pecuniary and enforcement issues is a vital consideration that could benefit the NPRM process. Additionally, the Administrator's approval of Nebraska as a DP warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, Nebraska has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor's enforcement-related interests may be best served by considering presentation consolidation with other enforcement-motivated requestors.

Ari Kirshenbaum, PhD

In his POR, Dr. Kirshenbaum identifies himself as a PhD researcher and Psychology professor emeritus who is presently engaged in "research related to cannabis-related impairment of the skills needed for motor vehicle operation." Kirshenbaum POR at 1. The requestor indicates that the current placement of marijuana in Schedule I presents mandatory procedural steps that can result in delays in conducting research. *Id.* at 2. Dr. Kirshenbaum's POR states that he is currently "co-leading a research study out of the University of California San Francisco (Medical School) that has been delayed for over a year due to the regulatory hurdles necessitated by [marijuana's] Schedule I designation." *Id.*

³⁰ Nebraska's alternative argument that standing under the APA, the CSA, and the CSA's implementing regulations is satisfied exclusively by virtue of the fact that the Administrator designated it as a participant misperceives the recommended decision hearing structure. Analogously, although all DEA immediate suspension enforcement hearings commence with the issuance of a charging document by the Administrator, assigning controlling weight to that preliminary decision and binding the ALJ thereby would render the hearing process under the APA as illusory. 21 U.S.C. § 811(a). That cannot be the intent of Congress. To be sure, decisions regarding standing (like all rulings and decisions made by an ALJ) are subject to the Administrator's review, but a final order that is consistent with the recommended decision is stronger than when the contrary occurs. *See generally, Morall v. DEA*, 412 F.3d 165, 177 (D.C. Cir. 2005) ("The Agency's departures from the ALJ's findings are vulnerable if they fail to reflect attentive consideration to the ALJ's decision.").

Dr. Kirshenbaum supports the rescheduling of marijuana into Schedule III so that his studies can be conducted more expeditiously. On the issue of SC One (aggrievement, adverse impact or Article III standing), Dr. Kirshenbaum does not specify how he would be “adversely affected or aggrieved” by the *promulgation* of the proposed rescheduling rule. Not only would the proposed rescheduling not adversely affect or aggrieve this requestor, but he wants it to happen quickly. Accordingly, consideration of SC One does not inure to this requestor’s benefit.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is within the scope of the NPRM (SC Three). Under SC Four (Meaningful Assistance/Consolidation Potential) Dr. Kirshenbaum offers his own testimony, which could potentially bring a knowledgeable and relevant perspective from academia. Additionally, the Administrator’s approval of Dr. Kirshenbaum as a DP warrants significant deference.

Upon a thoughtful balance of the four SC Factors, Dr. Kirshenbaum has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve him. Placing appropriate weight on Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Consideration of the other SC Factors (in particular, SC Four, in light of the Administrator’s designation) lend some support to allowing this requestor’s participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to his presentation in this recommended decision. Dr. Kirshenbaum may wish to consider the prospect of presentation consolidation with other academic/medical professional requestors who are supportive of the NPRM.

Office of Cannabis Ombudsman, State of Connecticut (OCO)

In its POR, OCO defines itself as “the first-in-the-nation independent state agency with a mission to protect and preserve the needs of medical cannabis patients.” OCO POR at 1-2. The POR explains that OCO is statutorily created and its focus is to provide assistance to

Connecticut residents [as] they navigate the [m]edical cannabis system through direct assistance; outreach and educational activities; meetings, facility visits and continuous communication with current and future suppliers; assessing and implementing needed improvements; and working with research centers,

universities and advocates to monitor and improve [the state] system and bring best-in-class standards to [Connecticut].

Id. at 2. OCO represents that it “generally supports the [NPRM] and removing marijuana from [S]chedule I” due to criminal and other consequences that stem from that designation. But it also says that it “has concerns with a [S]chedule III placement” because state residents seeking medical marijuana could be “confused if cannabis becomes akin to Tylenol 3 and other pharmaceuticals in [S]chedule III.” *Id.* at 3. Confusingly, OCO also expresses additional “concerns” that existing regulations (which apply to all Schedules) “could increase the price and decrease the availability of medicinal cannabis if enforced by DEA, which is currently not the case.”³¹ *Id.* Lastly, OCO is apparently also opposed to quotas and other controls that could be required to bring a Schedule III-marijuana in line with the terms of the Single Convention. *Id.* Thus, OCO is apparently “generally” supportive of rescheduling marijuana, but not supportive of controls that could be required to comply with U.S. treaty obligations.

While Connecticut is doubtless a relatively populous state, the true number of OCO’s beneficiaries cannot be readily ascertained from its POR. Consequently, OCO’s position on the NPRM renders the issue of associational standing irrelevant. The POR does not specify how OCO or any of the state residents that utilize its services would be “adversely affected or aggrieved” by the *promulgation* of the proposed rescheduling rule. In fact, although OCO has taken an arguably nuanced view of the NPRM, it has made it clear that it is “generally” supportive. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor’s benefit.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is generally within the proper scope of the NPRM (SC Three). The POR’s demonstration under SC Four (Meaningful Assistance/Consolidation Potential) supplies little insight into whether it has sources of authoritative information at its disposal that could prove helpful in the decision the Agency must make beyond the perspective of this independent agency within the State of Connecticut,³² but as an independent agency with a mission that is so closely aligned with the

³¹ Enforcement (or past/future Congressional riders precluding enforcement) is not an issue within the scope of the NPRM.

³² It is unclear as to whether OCO is authorized to speak on behalf of the State of Connecticut.

subject of the NPRM, its input certainly carries with it the potential to render a valuable contribution. Beyond all that, the Administrator's approval of OCO as a DP warrants significant deference.

Upon a thoughtful balance of the four SC Factors, OCO has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve its own interests or the interests of those on whose behalf it advocates. Placing appropriate weight on Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Consideration of the other SC Factors (in particular, SC Four, as evidenced by the Administrator's designation) lend some support to allowing this requestor's participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision. This requestor may wish to consider presentation consolidation with other DPs focused on enhancing marijuana access to specific groups and who support promulgation of the NPRM.

Tennessee Bureau of Investigation (TBI)

TBI's POR provides the following account of its duties and mission:

The [TBI] is Tennessee's lead investigative agency with original jurisdiction over drug enforcement and the primary agency for forensic science services for law enforcement in the State. This includes operating the Tennessee Dangerous Drugs Task Force, which collaborates with federal agencies (including the DEA) to combat drug crimes across the State. TBI both investigates and enforces federal and state drug-related offenses, including marijuana offenses.

TBI POR at 1. Additionally, TBI represents that its forensic crime labs process over 30,000 drug submissions annually, many of which involve marijuana. *Id.* at 2. TBI posits that the proposed rescheduling would increase the prevalence of marijuana, would strain its drug-enforcement activities, and result in an immediate and adverse impact on TBI's mission. More specifically, according to TBI, the promulgation of the NPRM would result in "significant time and resources to reassess enforcement priorities, personnel assignments, and adjust asset allocations" *Id.* at 3.

Inasmuch as its representations depict the potential for pecuniary costs and (in its view) public safety challenges, this requestor has established standing under Article III, and its position militates strongly in favor of standing under SC One (aggrievement, adverse impact or Article III standing).

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is squarely within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential) it is self-evident that the official view of the primary drug law enforcement entity in a state regarding the impact of the NPRM on its pecuniary, training and enforcement issues is a vital consideration that could benefit the NPRM process. Additionally, the Administrator's approval of TBI as a DP warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, TBI has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor may be well served to consider presentation consolidation with other enforcement focused DPs who oppose the proposed rescheduling.

Village Farms International (VFI)

According to its POR, VFI is a large-scale supplier of products who either is or seeks to be a supplier of marijuana. The requestor broadly describes its mission as seeking "to improve life's journey for the wellbeing of humankind and the earth on which we live." VFI POR at 1. Very broad, to be sure. As its basis for APA standing, VFI represents that it intends to enter the U.S. marijuana market and that the proposed rescheduling of marijuana to Schedule III would "facilitate its goals of researching, manufacturing, importing, and exporting marijuana for scientific and medical purposes consistent with state and federal law ..." and that those goals are hindered by the current Schedule I placement. *Id.* at 4. In VFI's view, numerous, specific regulatory barriers would soften if the NPRM succeeds, and those barriers would include easier access to research, gentler requirements for inventory, export, and ordering. *Id.* at 4-5. These ameliorations, in this requestor's opinion, would result in higher profits and more efficiencies.

The POR has convincingly outlined how placing marijuana in Schedule III would be helpful to its commercial interests, and is likewise clear that its ultimate objective is descheduling or scheduling to an even less restrictive level than Schedule III. The requestor views the NPRM as "an incremental step toward optimizing the U.S.'s legal approach to marijuana" (read: legalization). *Id.* at 6. None of VFI's expanded objectives are contemplated by the present NPRM. The POR regarding this requestor does not specify how it would be

“adversely affected or aggrieved” by the *promulgation* of the proposed rescheduling rule, but rather, outlines how its research and pecuniary interests would be advanced by rescheduling. This is a requestor who aspires to pursue the purported benefits of marijuana for commercial use. Thus, this requestor has not demonstrated that it would be adversely affected or aggrieved by promulgation of the NPRM, but that it will not accrue the potential benefits it aspires to upon the failure of the NPRM. Rescheduling presents a potential benefit to this requestor, but declining to do so will not adversely affect its interests beyond the status quo. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor’s benefit.

Under SC Two (compliance with procedural directives), the RFH was apparently timely, and the POR is clear in its support of the proposed rescheduling (albeit as an incremental measure), discusses the issues upon which it desires to be heard, and adequately outlines its position. On the whole, this requestor has complied with the relevant Preliminary Order and the procedural directives of the Agency in the NPRM. Thus, SC Two does not disfavor APA standing. Similarly, inasmuch as the POR is mostly focused on the rescheduling depicted in the NPRM and its potential impact on its commercial interests, SC Three (within the scope of the NPRM) militates in favor a grant of APA standing for this requestor.

Regarding SC Four (Meaningful Assistance/Consolidation Potential), a reasonable reading of the POR depicts an enterprise with considerable experience in supplying agricultural products on a large scale, a likely result of rescheduling marijuana into medicine. Such input has the potential to bring valuable perspectives to the rescheduling equation. Beyond that, the Administrator has identified this requestor as a DP.

Upon a thoughtful balance of the four SC Factors, VFI has certainly not adequately demonstrated that promulgation of the NPRM will adversely affect or aggrieve its interests within the unambiguous, directive terms of the regulations. Upon consideration of the powerful Factor One, this requestor has **NOT DEMONSTRATED STANDING BUT MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS.**³³ Analyzing the other SC Factors (in particular, SC Four, as evidenced by the nature and scale of this requestor’s business,

³³ VFI’s unsupported accusation that the DEA is an improper advocate or sponsor of its own NPRM adds nothing to the standing equation (at least on the present record and at this procedural juncture). The issues at stake in these proceedings are too important to devote time and attention to *ad hominem* distractions. This accusation has also been set forth in a separate motion, which will be addressed in a separate order.

as well as the Administrator's designation) militate in favor of VFI's participation in these proceedings, but the issue of standing may properly be factored into the weight accorded to its presentation in this recommended decision. Inasmuch as VFI shares a pecuniary and commercial concerns with other requestors, it may be prudent for this requestor to a consolidation of presentations with other commercially-motivated DPs who also support the NPRM.

Smart Approaches to Marijuana (SAM)

SAM's POR describes the organization as "a bipartisan alliance of organizations and individuals dedicated to a health-first approach to marijuana ... comprised of medial doctors, lawmakers, treatment providers, preventionists, teachers, law enforcement officers who seek a middle road between incarceration and legalization." SAM POR at 1. It defines its mission as "equip[ing] policymakers with commonsense proposals, based in reputable science, to promote public health and decrease marijuana use and its consequences." *Id.*

By the terms of its POR, SAM presents itself as an advocacy organization. The POR references "organizations," but has made no representations that would sustain associational standing. Thus, the standing justification of this requestor are exclusively founded in its claim that it would be aggrieved and adversely affected by the potential affect rescheduling would have on its training and advocacy expenditures as a marijuana-skeptical material and lecturing source.³⁴ Inasmuch as this requestor has adequately demonstrated that promulgation of this

³⁴ SAM's alternate theory, *to wit*, that it is somehow magically endowed with APA standing by virtue of the fact that the Administrator sent a DP letter is singularly unpersuasive. SAM POR at 2. First, the regulations apply to DEA – all of DEA. While it is possible to apply to the Administrator "for an exception to the application of any [regulation] by filing a written request . . . stating the reasons for such an exception," no such written request granted by the Administrator is part of the present record. 21 C.F.R. § 1307.03. Beyond that, SAM's theory misperceives the structure of adjudications under the APA, the CSA, and the CSA's implementing regulations. As discussed elsewhere in this order, Congress was crystal clear in placing APA proceedings as a condition precedent to rescheduling by the Agency. 21 U.S.C. § 811(a). Determinations as to standing fixed by the Administrator at the outset of the hearing would obstruct the ALJ's authority to issue a report including a statement of all "findings and conclusions, and the reasons or basis therefor, on all the material issues of fact, law, or discretion as presented on the record [and] the appropriate rule" 5 U.S.C. § 557(c). Analogously, although all DEA immediate suspension enforcement hearings commence with the issuance of a charging document by the Administrator, assigning controlling weight to that preliminary decision and binding the ALJ thereby would render the hearing process under the APA as illusory. 21 U.S.C. § 811(a). That cannot be the intent of Congress. To be sure, decisions regarding standing (like all rulings and decisions made by an ALJ) are subject to the Administrator's review, but a final order that is consistent with the recommended decision is stronger than when the contrary occurs. *See generally, Morall v. DEA*, 412 F.3d 165, 177 (D.C. Cir. 2005) ("The Agency's departures from the ALJ's findings are vulnerable if they fail to reflect attentive consideration to the ALJ's decision.").

NPRM would adversely affect its budget and mission, SC One (aggrievement, adverse impact or Article III standing) militates in favor of APA standing.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential) it is self-evident that the official view of an advocacy entity that purports to have wide-ranging, bipartisan support and can show adverse impact as a direct result of the proposed rescheduling action has the potential for significant, relevant input here. Further, the Administrator's approval of SAM as a DP (while not necessarily controlling) warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, SAM has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor may wish to consider the option of presentation consolidation with other DP advocacy groups who do not favor the proposed rescheduling.

National Cannabis Industry Association (NCIA)

The POR filed by NCIA describes itself as “the oldest, largest, and most inclusive [tax-exempt non-profit] trade association representing the legal cannabis industry.” NCIA POR at 2. The POR further represents that NCIA’s “membership is composed of hundred of businesses from all sectors of the industry—from state-licensed cannabis businesses to legal hemp product manufacturers to the wide range of ancillary businesses serving the industry” and styles itself as “the voice of Main Street Cannabis.” *Id.*

NCIA has put forward its APA standing argument in essentially two prongs. The first is not persuasive, but much of the second prong is. Both prongs are underpinned by an associational standing theory. That is, that its standing derives from its theory that one or more of its members would have standing to sue in their own right, the interests to be protected are germane to the organization’s purpose, and the result the organization is pursuing requires the participation of individual members in the lawsuit. *Fund Democracy*, 278 F.3d at 25 (citing *Friends of the Earth*, 528 U.S. at 181).

The first prong is that it (and presumably its members) support rescheduling into Schedule III because that action “would both lessen criminal penalties and preclude the application of [Internal Revenue Code § 280E] ... to marijuana businesses” that are not currently operating in violation of applicable state laws. NCIA POR at 6. Inasmuch as this prong supports the proposed rescheduling action, it would not, at least in this regard adversely affect or aggrieve its membership, and does not further its standing argument under SC One (aggrievement, adverse impact or Article III standing).

The other theory of standing is both more nuanced and more persuasive. NCIA posits that a number of its members would be adversely affected by a new definition of tetrahydrocannabinol which is incorporated into the NPRM. Without engaging in a deep dive into the merits of this issue, NCIA argues that the NPRM definition “could cause currently unscheduled [n]on-[i]ntoxicating [c]annabinoids to be designated as prohibited Scheduled I controlled substances without [additional] scheduling actions” on the part of DEA. NCIA POR at 4. A significant weakness in this position is that NCIA has not specifically alleged that any of its members are currently utilizing any particular substances that would be affected (a deficit that could conceivably undermine its standing argument in this regard). However, NCIA’s POR contains the following representation:

NCIA is adversely affected or aggrieved by the [NPRM] because the simultaneous scheduling of certain [n]on-intoxicating [c]annabinoids as Schedule I substances through the [NPRM’s] proposed revisions to the definition of THC would make one or more NCIA members’ businesses federally illegal for the first time.

Id. at 3 (internal quotation marks omitted). Thus, based on the fact that this requestor has alleged that it is properly in a position to exercise associational standing with several of its members who could potentially have their present business enterprises rendered illegal by promulgation of the NPRM, SC One favors standing on this narrow issue.³⁵

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order and the procedural directives of the Agency. Likewise, the subject matter of the POR is somewhat within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful

³⁵ Contrariwise, NCIA’s more speculative arguments regarding what the Agency may do in the future, based on its pronouncements in the past and other interpretations, are unpersuasive and beyond the scope of the NPRM. See e.g., *Id.* at 5.

Assistance/Consolidation Potential), as described in its POR, it seems that NCIA would have the means at its disposal to provide qualified witnesses among its large and diverse membership, and that the commercial perspective available to it would be helpful to the adjudication of this NPRM. That said, its commercial perspective may lend itself readily and effectively to a consolidation with other DPs. Additionally, the Administrator's approval of NCIA as a DP warrants significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, NCIA has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS.**

Inasmuch as this requestor shares a pecuniary and commercial concerns with other requestors, it may be prudent to a consolidation of presentations with other commercially-motivated DPs who also support the NPRM.

Ellen Brown

While Ellen Brown's POR references her position as Research Subcommittee Chair of the Massachusetts Cannabis Advisory Board (MCAB), there is no indication therein that she is authorized (or seeking) to speak for that body.³⁶ Indeed, the POR is written in the first person, and focuses, not on the MCAB, but on her own experiences. Ms. Brown indicates that her position on the MCAB Research Subcommittee has provided her with some exposure to veterans, but evidently, she is not in a group authorized to speak on any behalf beyond her own. Ms. Brown further provides that she is a veteran, and as one under the care of the Veteran's Administration (the VA), she has "personally been aggrieved" by marijuana's current Schedule I placement and is in favor of the proposed rescheduling action set forth in the NPRM. Brown POR at 2.

Ms. Brown's POR does not specify how she would be "adversely affected or aggrieved" by the *promulgation* of the proposed rescheduling rule. It is her stated position that she and other veterans would markedly benefit by DEA's embracement of the NPRM and rescheduling of marijuana to Schedule III, thereby opening marijuana treatment avenues. *Id.* Thus, this requestor has not demonstrated that she would be adversely affected or aggrieved by

³⁶ To the extent this conclusion is incorrect and Ms. Brown is indeed authorized to speak for MCAB, that body or Ms. Brown may file a clarification within five (5) business days from the receipt of this order with a request to reconsider.

promulgation of the NPRM. Rescheduling presents a potential benefit to this requestor and (at least in her view) other veterans. Accordingly, consideration of SC One (aggrievement, adverse impact or Article III standing) does not inure to this requestor's benefit.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is generally responsive, and in some respects consistent with the Preliminary Order as well as the procedural directives of the Agency. Likewise, the subject matter of the POR is within the proper scope of the NPRM to some extent (SC Three). The POR's demonstration under SC Four (Meaningful Assistance/Consolidation Potential) is difficult to gauge. Although Ms. Brown represents that she has spoken to some veterans interested in exploring the benefits of marijuana as medicine, there is no indication about the number of veterans or anything beyond some limited anecdotal, generalized representations. That the Administrator approved Ms. Brown status as DP's is entitled to significant deference, but balancing the powerful SC One and the other SC Factors, Ms. Brown has not made a sufficient (standing or evidentiary) presentation to warrant her participation in these proceedings.

Upon a thoughtful balance of the four SC Factors Ms. Brown has not demonstrated that promulgation of the NPRM will adversely affect or aggrieve her own interests and has noticed little beyond her own experience and expectations about the potential benefits of rescheduling marijuana as sought by the DEA. Placing appropriate regulatory emphasis on the powerful Factor One, this requestor has **NOT DEMONSTRATED STANDING AND MAY NOT INDEPENDENTLY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. Ms. Brown's POR efforts and input may be better suited to consolidation with another DP who has presented a sufficient showing to warrant participation.

Drug Enforcement Association of Federal Narcotics Agents (DEAFNA)

The POR filed on behalf of DEAFNA describes the association as a “[l]aw [e]nforcement [f]raternal [o]rganization representing active and retired DEA Special Agents, Diversion Investigators, Intelligence Research Specialists, and other DEA [p]ersonnel.” DEAFNA POR at 2.

DEAFNA's basis for standing is that the rescheduling “has a direct impact on [its] members' ability to implement the necessary regulatory controls which will take years to implement and will come at an unreasonable financial cost.” *Id.* This requestor is against the proposed rescheduling because it would present “a significant shift in federal drug policy with

significant implications for ... the ability of law enforcement agencies to protect the public.” *Id.* at 3. As noted *supra*, “[a]n association only has standing to bring suit on behalf of its members when its members would otherwise have standing to sue in their own right, the interests [the association] seeks to protect are germane to the organization’s purpose, and neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit.” *Fund Democracy*, 278 F.3d at 25 (citing *Friends of the Earth*, 528 U.S. at 181). Here, inasmuch as DEAFNA’s members, as specialized public servants engaged in the regulation and enforcement actions under the CSA, could potentially demonstrate adverse effect from the promulgation of the NPRM, the action is clearly germane to DEAFNA’s purpose, and the members of the organization are not required participants in the action. Here, the interests cited by DEAFNA, at least as articulated as adverse (that is—at least in its view—the potentially adverse impact rescheduling could have on the law enforcement efforts to enforce driving and other impairment-related and fit-for-duty laws regularly enforced by many of its members), could conceivably be adversely impacted by promulgation of the NPRM. Accordingly, SC One favors standing in this case.

With respect to SC Two (compliance with procedural directives), as proffered, the RFH was apparently timely, and the POR is responsive, and consistent with the Preliminary Order as well as the procedural directives of the Agency. Likewise, the subject matter of the POR is within the proper scope of the NPRM (SC Three). On the issue of SC Four (Meaningful Assistance/Consolidation Potential), this requestor organization (at least as noticed in its POR) specializes in law enforcement in the field of controlled substances. It would be reasonable to assume that this requestor has access to members with the potential to speak authoritatively on the listed issues of concern, a law enforcement perspective (particularly this highly-specialized law enforcement perspective) is quite valuable, and even beyond all that, that the Administrator approved DEAFNA’s status as DP’s is entitled to significant deference.

Accordingly, inasmuch as all four of the SCs favor standing, this DP has **ESTABLISHED STANDING AND MAY CONTINUE TO PARTICIPATE IN THESE PROCEEDINGS**. This requestor should strongly consider the option of presentation consolidation with other enforcement-motivated DPs who also disfavor the NPRM.

On Procedure

In accordance with my authority to regulate the course of the hearing,³⁷ the following procedures are herein implemented to ensure fair and orderly proceedings. While the Government, as the burdened party, may present multiple witnesses, each of the remaining DPs (absent leave to the contrary granted by this tribunal) may present the testimony of a single witness. Documentary evidence and proposed witnesses from all the Parties must be disclosed in advance in a written disclosure (Prehearing Statement) as outlined below. No evidence will be admitted to the record without a proper foundation presented at the hearing on the merits.

Within the discretion of the tribunal, and to the extent practicable, each of the Parties will present testimonial and documentary evidence as set forth below.

The Government, as the burdened party, will present its evidence first. Those DPs who support the NPRM (Pro-Rescheduling DPs) will present evidence following the conclusion of the Government's case. The DPs who oppose the NPRM (Anti-Rescheduling DPs) will present evidence following the conclusion of the Pro-Rescheduling DPs' presentations. All DPs (Pro and Anti) will be limited to a single witness each, with direct examination limited to no more than approximately ninety (90) minutes (excluding cross-examination). Anti-Rescheduling DPs may cross-examine all Government witnesses and all Pro-Rescheduling witnesses. Witnesses presented by the Anti-Rescheduling DPs may be cross-examined by the Government and Pro-Rescheduling DPs. In all cases, cross-examination will be limited to approximately twenty (20) minutes per witness for each authorized cross-examiner. Within the further discretion of the tribunal, presentations may be grouped (or even consolidated) by the tribunal in accordance with commonly-expressed viewpoints as set forth in the Parties' respective PORs.

Any Party (to include the Government) who is unprepared to proceed on the date(s) scheduled at the preliminary hearing (with the input of that Party) may forfeit his/her/its ability to present the scheduled evidence or examination.

It is herein **ORDERED** that the Parties, no later than **2:00 p.m. Eastern Time (ET) on November 26, 2024**, shall electronically file with this tribunal and serve on each other, a Prehearing Statement³⁸ containing the following sections:

³⁷ 5 U.S.C. § 556(c)(5); 21 C.F.R. § 1316.52.

³⁸ Absent advance leave by this tribunal on a motion supported by good cause, all filed documents (other than noticed proposed exhibits offered by either party on the merits) *shall be limited to fifty (50) pages* (utilizing 12-point characters and 1-inch margins).

1. **Witnesses.** Names, *curriculum vitae*, and current addresses of all witnesses whose testimony is sought to be presented by each of the Parties.
2. **Summary of Testimony.** Brief summary of the testimony of each witness. The summaries are to state what the testimony will be, rather than merely list the areas to be covered. Testimony not disclosed may be subject to exclusion.
3. **Documents.** A list noticing all documentary evidence, including affidavits and other proposed exhibits, intended to be offered into evidence, specifying the number of pages in each. Each proposed exhibit is to be marked for identification and numbered as follows: (“[name of Party]-Exh. No. ## (ID)”).
4. **Hearing Date Availability.** The NPRM and GNoH in this matter fixes the place of hearing as the DEA Hearing Facility in Arlington, Virginia. The Government and the Parties are expected to provide their representatives’ and their witnesses’ availability for the months of January through February 2025³⁹ at the Preliminary Hearing.
5. **District Court Intervention.** To the extent practicable, each Party should indicate whether he/she/it presently intends to seek the intervention of a U.S. District Court in accordance with *Axon Enterprise, Inc. v. FTC*, 598 U.S. 175 (2023).

It is further **ORDERED** that, in accordance with 21 C.F.R. § 1316.64, **a Preliminary Hearing⁴⁰ in this matter will be conducted on December 2, 2024, at 9:30 a.m. ET in the North Courtroom⁴¹ at the DEA Hearing Facility**, at 700 Army Navy Drive, Arlington, Virginia, 22202.⁴²

It is further **ORDERED** that all proceedings will be governed by the provisions of 21 C.F.R. §§ 1316.41-1316.68.⁴³ Your attention is specifically directed to 21 C.F.R. § 1316.45, which provides, *inter alia*, that “[d]ocuments shall be dated and deemed filed upon receipt by the

³⁹ 21 C.F.R. § 1301.45.

⁴⁰ 21 C.F.R. § 1316.

⁴¹ As set forth in the Preliminary Order, the courtrooms at the DEA Hearing Facility are spacious and modern, but not unlimited. Accordingly, in view of the potentially high number of hearing participants, it is anticipated that admission to the preliminary hearing will be limited to representatives (no more than two, preferably one) and credentialed media as designated by the Agency. The Administrator has directed the proceedings will be livestreamed to afford those physically outside the courtroom an opportunity to observe the proceedings. Naturally, witnesses will be admitted to the courtroom to testify at the merits hearings at times where their testimony is scheduled. No cell phone use by anyone will be permitted in the courtroom at any hearing conducted in this matter. The highest level of decorum will be maintained at all times during all hearings, and court attire is required for anyone participating in any capacity. All representative appearances will be live (not virtual) throughout, and all representatives must plan to arrive sufficiently early to allow security processing through the DEA Visitor Center, which is collocated with the DEA Hearing Facility at 700 Army Navy Drive, Arlington, Virginia, 22202.

⁴² Logistical issues will be coordinated by Law Clerk Laila Mogharabi, Esq., who can be contacted at (202) 307-8188 and at ECF-DEA@dea.gov.

⁴³ Additional helpful information regarding DEA administrative proceedings may be found at the OALJ website, <https://www.dea.gov/administrative-law-judges>.

Hearing Clerk.” Documents (other than proposed exhibits) may be filed electronically or by hard copy. Only one method of document filing may be utilized.

Electronic Filing: The strongly preferred method of filing correspondence in these proceedings is as a PDF attachment via email to the DEA Judicial Mailbox (**ECF-DEA@dea.gov**). The forwarding email on all electronically filed correspondence must indicate that it was simultaneously served on the opposing party via email. The Respondent must ensure that all documents filed with the DEA Judicial Mailbox are simultaneously served on the Government Mailbox at (**dea.registration.litigation@dea.gov**). Any request(s) to modify email addresses of a party or counsel must be made on notice to this tribunal and the opposing party. The email receipt date reflected by the DEA Judicial Mailbox server shall conclusively control all issues related to the date of service of all filed correspondence, provided however, that correspondence received after 5:00 p.m., local Washington, D.C. time, will be deemed to have been received on the following business day. Note: While email is utilized as the method to forward documents for filing—as attachments—no substantive matter communicated through the body of a forwarding email will be considered. The parties are directed to refrain from including social security numbers or personally identifiable information in electronically-filed documents. Proposed evidentiary exhibits will not be accepted via electronic filing. Details regarding evidentiary exhibit filing will be the subject of a subsequent order.

Hard Copy Filing: Alternatively, correspondence may be filed in hard-copy form. Hard-copy filings must be served in triplicate and addressed to my attention at: **The DEA Office of Administrative Law Judges, 8701 Morrisette Drive, Springfield, Virginia 22152**. Because the DEA Hearing Facility is not physically collocated with the DEA mailing address, hard copy filings must be posted sufficiently in advance of the due date to assure timely receipt by this office.

Failure to timely file a prehearing statement that complies with the directions provided above may result in a sanction, including (but not limited to) a waiver of hearing and an implied withdrawal of a request for participation. Prehearing statements should not include motions, which should be filed separately.⁴⁴

⁴⁴ A prehearing ruling setting deadlines will be issued after the prehearing conference.

It is further **ORDERED** that any requests for extension of time to file must be made by written motion sufficiently in advance of scheduled deadlines to be considered and ruled upon.

Dated: November 19, 2024

JOHN

MULROONEY

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JOHN MULROONEY

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JOHN J. MULROONEY, II
Chief Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on November 19, 2024 caused a copy of the foregoing to be delivered to the following recipients: (1) James J. Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; Jarrett T. Lonich, Esq., Counsel for the Government, via email at jarrett.t.lonich@dea.gov; and S. Taylor Johnston, Esq., Counsel for the Government, via email at stephen.t.johnston@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington, Esq., Counsel for Village Farms International, via email at spennington@porterwright.com; and Tristan Cavanaugh, Esq., Counsel for Village Farms International, via email at tcavanaugh@porterwright.com; (4) Nikolas S. Komyati, Esq., Counsel for National Cannabis Industry Association, via email at nkomyati@foxrothschild.com; William Bogot, Esq., Counsel for National Cannabis Industry Association, via email at wbogot@foxrothschild.com; and Khurshid Khoja, Esq., Counsel for National Cannabis Industry Association, via email at khurshid@greenbridgelaw.com; (5) John Jones and Dante Picazo for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (6) Andrew J. Kline, Esq., Counsel for Hemp for Victory, AKline@perkinscoie.com; and Abdul Kallon, Esq., Counsel for Hemp for Victory, via email at and AKallon@perkinscoie.com; (7) Erin Gorman Kirk for the State of Connecticut, via email at erin.kirk@ct.gov; (8) Ellen Brown for Massachusetts Cannabis Advisory Board, via email at ellen@greenpathtraining.com; (9) Shanetha Lewis for Veterans Initiative 22, via email at info@veteransinitiative22.com; (10) Jason Castro, Esq., Counsel for The Doc App., Inc. d/b/a My Florida Green, via email at jasoncastro@myfloridagreen.com; (11) Kelly Fair, Esq., Counsel for The Commonwealth Project, via email at Kelly.Fair@dentons.com; (12) Rafe Petersen, Esq., Counsel for Ari Kirshenbaum, via email at Rafe.Petersen@hkclaw.com; (13) David G. Evans, Esq., Counsel for Cannabis Industry Victims Educating Litigators, Community Anti-Drug Coalitions of America, Phillip Drum, Kenneth Finn, International Academy on the Science and Impacts of Cannabis, and National Drug and Alcohol Screening Association, via email at thinkon908@aol.com; (14) Patrick Philbin, Esq., Counsel for Smart Approaches to Marijuana, via email at pphilbin@torridonlaw.com; and Chase Harrington, Esq., Counsel for Smart Approaches to Marijuana, via email at charrington@torridonlaw.com; (15) Stephanie E. Masker, Esq., Counsel for National Transportation Safety Board, via email at stephanie.masker@ntsb.gov; (16) Eric Hamilton, Esq., Counsel for the State of Nebraska, via email at eric.hamilton@nebraska.gov; and Zachary Viglianco, Esq., for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (17) Gene Voegtlin for International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (18) Gregory J. Cherundolo for Drug

Enforcement Association of Federal Narcotics Agents, via email at executive.director@afna.org; (19) Reed N. Smith, Esq., Counsel for the Tennessee Bureau of Investigation, via email at Reed.Smith@ag.tn.gov; and Jacob Durst, Esq., Counsel for Tennessee Bureau of Investigation, via email at Jacob.Durst@ag.tn.gov; and (20) Jim Skinner for National Sheriff's Association, via email at sheriffskinner@collincountytx.gov and ykaraman@sheriffs.org.

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Quinn Fox
Staff Assistant to the Chief Judge
Office of Administrative Law Judges

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

ORDER DENYING MOTION TO INTERVENE (DDPR)

On May 21, 2024, the United States Department of Justice through the Drug Enforcement Administration (DEA or Agency) issued a notice of proposed rulemaking (NPRM) proposing to transfer marijuana from Schedule I of the Controlled Substances Act (CSA) to Schedule III. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 44597, 44597 (2024). Following the publication of the NPRM, the DEA Administrator determined that in-person hearing proceedings would be appropriate, and in an order dated August 29, 2024, fixed a December 2, 2024 commencement date. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 70148, 70148-49 (2024). Subsequently, the Administrator designated a subset of twenty-five (25) individuals and organizations (evidently culled from a larger group of requestors) to participate in the hearing (Designated Participants or DPs). The DPs were evidently each notified of their participation status by a separate email.

I was designated by the Administrator¹ to preside over the hearing proceedings, but was not involved in or apprised of the process utilized to select the DPs. In an order dated November 19, 2024 (the Standing Order), based on submissions by the DPs, I made determinations regarding standing and inclusion in these proceedings by applying the statutory and regulatory guideposts supplied by Congress and the CSA and its implementing regulations. In the Standing Order, the overwhelming majority of DPs maintained their status as participants, but standing assessments were reached regarding a future discretionary decision as to the potential weight to be assigned in the recommended decision.

¹ 21 C.F.R. § 1316.52.

On November 13, 2024, Doctors for Drug Policy Reform and Bryon Adinoff (collectively, DDPR), a filed a thoughtful motion bearing the caption “Non-Party D4DPR’s Motion to Intervene and Request for Final Appealable Determination” (Motion to Intervene or MTI) seeking a final order memorializing the decision that caused its lack of its own invitational email from the Administrator, as well as an order from this tribunal authorizing its inclusion among the DPs notwithstanding her decision.

In its MTI, DDPR expends much effort into extolling its virtues (of which there are undoubtedly many) and pointing out how any marijuana rescheduling hearing would exponentially benefit from its participation. However, as explained in more detail in the Standing Order issued by this tribunal, that is not the full extent of the inquiry. *City of San Antonio v. Civil Aeronautics Board*, 374 F.2d 326, 329 (D.C. Cir. 1967) (“No principle [of] administrative law is more firmly established than that of agency control of its own calendar.”). The Agency is endowed with the right to place reasonable limits on the number of participants in a given APA hearing. *Id.* Which is, when reduced to its essence, precisely what the Administrator did in exercising her discretion in determining the number and nature of participants. To be sure, thousands upon thousands of individuals and entities across the country could add value to the issues to be decided here, but they cannot all be included.

Regarding the issuance of a final, appealable order from the Administrator, it is useful to view the current dynamic in the backdrop of the Administrative Procedure Act (APA) and the CSA’s implementing regulations. The Administrative Law Judge (ALJ) is appointed by the DEA Administrator. 21 C.F.R. § 1316.52. The ALJ’s “functions ... commence upon his designation and terminate upon the certification of the record to the Administrator.” *Id.* Thus, the time the DPs were selected preceded my authority to act on the case. Even more importantly, in the APA, Congress decreed that “[o]n appeal from or review of the [ALJ’s recommended decision] the agency has all the powers which it would have in making the [recommended decision] ... except as it may limit the issues on notice or by rule.” 5 U.S.C. § 557(b). Appeals flow *from the ALJ to the Administrator*, not the other way around. I have not been designated to review the Administrator’s prehearing actions on this matter or the manner in which her DP decisions were reached, issued, or not issued.² The Administrator exercised her discretion to fix

² See *SEC v. Chenery Corp.*, 318 U.S. 80, 87 (1943) (“The grounds upon which an administrative order must be judged are those upon which the record discloses that its action was based.”). As I have discussed in other orders,

the number of DPs to be included, and to expand that number would effectively overrule her decision and exceed the proper and logical role of the ALJ under the APA and the CSA.³

Accordingly, no action can or will be taken on DDPR's Motion to Intervene.

Dated: November 21, 2024

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JOHN J. MULROONEY, II
Chief Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on November 21, 2024 caused a copy of the foregoing to be delivered to the following recipients: (1) James J. Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; Jarrett T. Lonich, Esq., Counsel for the Government, via email at jarrett.t.lonich@dea.gov; and S. Taylor Johnston, Esq., Counsel for the Government, via email at stephen.t.johnston@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington, Esq., Counsel for Village Farms International, via email at spennington@porterwright.com; and Tristan Cavanaugh, Esq., Counsel for Village Farms International, via email at tcavanaugh@porterwright.com; (4) Nikolas S. Komyati, Esq., Counsel for National Cannabis Industry Association, via email at nkomyati@foxrothschild.com; William Bogot, Esq., Counsel for National Cannabis Industry Association, via email at wbogot@foxrothschild.com; and Khurshid Khoja, Esq., Counsel for National Cannabis Industry Association, via email at khurshid@greenbridgelaw.com; (5) John Jones and Dante Picazo for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (6) Andrew J. Kline, Esq., Counsel for Hemp for Victory, AKline@perkinscoie.com; and Abdul Kallon, Esq., Counsel for Hemp for Victory, via email at and AKallon@perkinscoie.com; (7) Shanetha Lewis for Veterans Initiative 22, via email at info@veteransinitiative22.com; (8) Kelly Fair, Esq., Counsel for The Commonwealth Project, via email at Kelly.Fair@dentons.com; (9) Rafe Petersen, Esq., Counsel for Ari Kirshenbaum, via email at Rafe.Petersen@hkllaw.com; (10) David G. Evans, Esq., Counsel for Cannabis Industry Victims Educating Litigators, Community Anti-Drug Coalitions of America, Phillip Drum, Kenneth Finn, International Academy on the Science and Impacts of Cannabis, and National Drug and Alcohol Screening Association, via email at thinkon908@aol.com; (11) Patrick Philbin, Esq., Counsel for Smart Approaches to Marijuana, via email at

while the decision to include or exclude a party arguably bears the hallmarks of a final agency action (5 U.S.C. § 702; 21 U.S.C. § 877), at least one Circuit Court is not altogether convinced that anything is really final and reviewable until the whole adjudication has run its course. *Miami-Luken, Inc. v. DEA*, 900 F.3d 738, 743 (6th Cir. 2018) (The court held that a subpoena decision is not rendered final merely because the agency's highest authority issued the decision prior to an ultimate disposition of the case.).

³ Admittedly, had the standing determination been deferred to await the action of the ALJ, matters would have been procedurally different and the Administrator could have exercised her unquestioned authority to review my ruling on the matter. But that is not the way the matter progressed.

pphilbin@torridonlaw.com; and Chase Harrington, Esq., Counsel for Smart Approaches to Marijuana, via email at charrington@torridonlaw.com; (12) Stephanie E. Masker, Esq., Counsel for National Transportation Safety Board, via email at stephanie.masker@ntsb.gov; (13) Eric Hamilton, Esq., Counsel for the State of Nebraska, via email at eric.hamilton@nebraska.gov; and Zachary Viglianco, Esq., for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (14) Gene Voegtlin for International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (15) Gregory J. Cherundolo for Drug Enforcement Association of Federal Narcotics Agents, via email at executive.director@afna.org; (16) Reed N. Smith, Esq., Counsel for the Tennessee Bureau of Investigation, via email at Reed.Smith@ag.tn.gov; and Jacob Durst, Esq., Counsel for Tennessee Bureau of Investigation, via email at Jacob.Durst@ag.tn.gov; and (17) Matthew Zorn, Esq., Counsel for Erin Gorman Kirk for the State of Connecticut, Counsel for Ellen Brown, and Counsel for Doctors for Drug Policy Reform and Bryon Adinoff, via email at mzorn@yettercoleman.com.

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Quinn Fox
Staff Assistant to the Chief Judge
Office of Administrative Law Judges

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

PREHEARING RULING

On December 2, 2024, a preliminary hearing (the Preliminary Hearing) was conducted in the above-captioned matter at the Drug Enforcement Administration (DEA or Agency) Hearing Facility in Arlington, Virginia. 21 C.F.R. § 1316.54. The Preliminary Hearing was held as part of ongoing hearing proceedings being conducted in connection with the publication of a notice of proposed rulemaking (NPRM) issued by the Department of Justice. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 44597 (2024). The NPRM seeks to move marijuana from Schedule I of the Controlled Substances Act (CSA) to Schedule III. *Id.* The DEA Administrator subsequently determined that a hearing was appropriate and published her own order (General Notice of Hearing or GNoH) stating as much. *Schedules of Controlled Substances: Rescheduling of Marijuana*, 89 Fed. Reg. 70148, 70148-49. The General Notice of Hearing fixed a December 2, 2024 commencement date. *Id.*

There has been a considerable level of spirited motion practice by the Designated Participants (and even numerous attempts from some outside that group). This Prehearing Ruling is issued pursuant to 21 C.F.R. § 1316.55.¹

I. Purpose

The NPRM and GNoH state that the purpose of this hearing is to receive factual evidence and expert opinion testimony regarding whether marijuana should be transferred to Schedule III

¹ The following cases were mentioned during the Preliminary Hearing: *Ester Mark, M.D.*, 86 Fed. Reg. 16760 (2021); *Gregg & Son Distributors*, 74 Fed. Reg. 17517 (2009); *Nicholas A. Sychak, d/b/a Medicap Pharmacy*, 65 Fed. Reg. 75959 (2000); *Loper Bright Enters. v. Raimondo*, 144 S. Ct. 2244 (2024); *Axon Enter., Inc. v. FTC*, 598 U.S. 175 (2023); *Kumho Tire Co. v. Carmichael*, 526 U.S. 137 (1999); *Miami-Luken, Inc. v. DEA*, 900 F.3d 738 (6th Cir. 2018); and *McClelland v. Andrus*, 606 F.2d 1278 (D.C. Cir. 1979).

under the CSA in accordance with 21 U.S.C. §§ 811, 812. 89 Fed. Reg. at 44599; 89 Fed. Reg. at 70149.

II. Witnesses

All of the parties have noticed their intention to present testimony at the hearing. The parties are reminded that testimony not summarized in prehearing statements may (and likely will) be excluded at the hearing on the merits. All parties should endeavor to ensure that their witnesses do not stray outside their areas of expertise. Witnesses may be afforded the opportunity to provide video teleconference (VTC) testimony should a request be filed with this tribunal **no later than 2:00 p.m. Eastern Time (ET) on December 13, 2024 (The Homework Date)**. Irrespective of whether a party has been granted leave to utilize VTC or will be present in court, any attorney/representative directing or cross-examining a witness must be physically present in the courtroom at the time of the examination.

The order of the parties' presentations is outlined *infra* and the following guidelines will apply to all parties, with the potential for some additional latitude afforded to the Government as the burdened party. **Each party will have ninety (90) minutes to present the testimony of their witness.** Before offering their witness, counsel **may present a two (2) minute opening statement** about their witness and any proposed exhibits to be sponsored through the witness. The parties are encouraged to consider whether there is merit in consolidation with other participants that have similar (or complimentary) litigation objectives, witnesses, and/or areas of interest. Consolidated parties will be afforded the opportunity to present the testimony of **up to two (2) witnesses** during the hearing, for a presentation not to exceed **one hundred and twenty (120) minutes**, should they avail themselves of the opportunity to consolidate.

At the conclusion of a party's presentation, counsel or the designated representative for that party may be afforded **either a ten (10) minute closing argument or the opportunity to submit a brief, not to exceed twenty-five (25) pages within five (5) business days** of their witness's presentation. This binary argument option will apply to all parties, regardless of the number of witnesses testifying.

The cross-examination of witnesses will generally be limited to matters covered on direct examination; however, if a party submits an affidavit or letter into evidence from a witness who also testifies in person, cross-examination as to matters referenced in the document may be

permitted, even if the witness does not refer to them in their direct testimony. As explained during the Preliminary Hearing, **cross-examination will be limited to twenty (20) minutes** for each party on the opposing side of the issue.

III. **Documents**

The parties have noticed their respective intentions to offer into evidence documents identified in their prehearing statements.² Further, all of the parties must serve each other with a copy (electronic or hardcopy) of the documents noticed in their respective prehearing statements no later than **January 3, 2025**. The parties are reminded that documents not timely supplied to the other Designated Participants or the tribunal, may (and likely will) be excluded at the hearing. The parties are further reminded that inasmuch as these are formal rulemaking proceedings, a foundation must be laid for recognition as an expert as well as for each and every proposed exhibit as a condition precedent for inclusion in the record. 21 C.F.R. § 1316.59. A limited number of affidavits³ may be received into the record, subject to the evidentiary weight

² For reasons that are not altogether apparent, although directed to do so in the November 19, 2024 Standing Order, the Government did not supply the complete list of documentary evidence it intended to offer into the record. Instead, the Government noticed a few documents and indicated below the line that notice of more documents could be forthcoming upon a supplemental filing date. In fairness to the Government's position, a supplemental prehearing statement date is not an uncommon feature of DEA administrative enforcement proceedings. There will be no supplemental prehearing statements in this formal rulemaking proceeding, and the Government is herein **DIRECTED** to furnish a complete list no later than **The Homework Date**. Further, as discussed at the Preliminary Hearing, the tribunal received several copies of proposed exhibits attached to the filings submitted in prehearing motion practice and none of those documents will be considered as part of the record. The process for submitting proposed exhibits for admission into the record is outlined later in this order.

³ During the Preliminary Hearing, the Government was granted leave to substitute an affidavit for the live testimony of one of its noticed witnesses, Heather Achbach, the Acting Section Chief of the DEA's Regulatory Drafting and Policy Support Section. This witness had been noticed to lay a foundation for comments (the Comments) filed by the American public in response to the NPRM. Mindful that this proposed exhibit has not yet been offered, for the planning purposes of all, as alluded to during the course of the Preliminary Hearing, it is quite unlikely that the Comments, which number well in excess of 43k, will be received into the hearing record. To be sure, NPRM comments play a vital role in the Administrative Procedure Act (APA) rulemaking process. They must be carefully analyzed by the proponent agency and responded to in detail in the final rule published in the Federal Register, but they are not admissible evidence at a hearing under the APA. 5 U.S.C. § 556(d) ("A party is entitled to present his case ... by documentary evidence ... and to conduct such cross-examination as may be required for a full and true disclosure of the facts."); *see also Attorney General's Manual on the APA* § 7(c) (The admission of evidence at an APA hearing "does not extend to presenting evidence in affidavit or other written form so as to deprive the agency or opposing parties of opportunity for cross-examination, nor so as to force them to assume the expense of calling the affiants for cross-examination."); *Basco v. Machin*, 514 F.3d 1177, 1182 (11th Cir. 2008); *J.A.M. Builders v. Herman*, 233 F.3d 1350, 1354 (11th Cir. 2000); *Keller v. Sullivan*, 928 F.2d 227, 230 (7th Cir. 1991); *Hoska v. Dep't of the Army*, 677 F.2d 131 (D.C. Cir. 1982); *Calhoun v. Bailar*, 626 F.2d 145, 149 (9th Cir. 1980). Neither are the Comments admissible evidence under the DEA's own regulations. 21 C.F.R. § 1316.59(a) ("The [ALJ] shall admit only evidence that is competent, relevant, material and not unduly repetitious."). The Comments were never intended by Congress to be part of the APA hearing process. The APA unequivocally directs that a "rule [may not

adjustment specified in the regulations. 21 C.F.R. § 1316.58(b) (“Affidavits admitted into evidence shall be considered in light of the lack of opportunity for cross-examination. . .”).

No later than the date fixed elsewhere in this order for the exchange of documents, each party is to file its noticed and proposed exhibits in the following manner: (1) each party will receive an email invitation to join the Department of Justice Enterprise File Sharing (JEFS) system, a secure commercial platform maintained by Box.com; (2) a party seeking to offer evidentiary exhibits must obtain a (free-of-charge) Box.com/JEFS account and must timely upload all proposed exhibits there; and (3) in addition to the electronic evidentiary submission on JEFS, each party must also timely provide three (3) complete sets of hard copies of all proposed exhibits to the Hearing Clerk.⁴ The submitted proposed exhibits (both hardcopy and electronic) must conform to the following specifications:

- Proposed exhibits must be pre-marked for identification with a docket number (e.g., Dkt. No. 23-42) and an exhibit number (e.g., [DP Name/Abbreviation] Ex. 1(ID) or Gov’t Ex. 1 (ID)).⁵
- The pages of each proposed exhibit must be numbered. In addition, the first page of each proposed exhibit must state the total number of pages contained therein.

be] issued except on consideration of the whole record or those parts thereof cited by a party and supported by and in accordance with the reliable, probative, and substantial evidence.” 5 U.S.C. § 556(d). The 43k+ comments are not evidence, they cannot be. Congress understood that when it drafted the APA, as did the Agency when it drafted its regulations. If the Comments are not admissible evidence they cannot be considered in the recommended decision. Admitting the Comments into a hearing record where they cannot be considered would indeed be a pointless exercise. On a more pragmatic level, to attempt to foist a gargantuan mass of inadmissible comments on the tribunal risks the appearance (even if subjectively unwarranted) of a dilatory tactic inflicted on the trier of fact by the agency that represents itself as the proponent of the rule. There is an additional dynamic that may bear some reflection. The DEA regulations require that in addition to the forwarding of evidence received into the record, where evidence is excluded, “if the excluded evidence consists of evidence in documentary or written form, a copy of such evidence *shall* be marked for identification and shall accompany the records as the offer of proof.” 21 C.F.R. § 1316.60 (emphasis supplied). Thus, as directed elsewhere in this order, by regulation, three (3) complete hardcopies of the Comments would have to be supplied to the tribunal at the time they are offered, and forwarded to the Administrator for her review, even if rejected here. Some additional reflection upon this strategy on the part of the Government may be prudent.

⁴ Due to DEA email capacity limitations, unless otherwise directed by the tribunal, proposed evidentiary exhibits will not be accepted through ECF. Proposed exhibits should be provided in hard copy format, as well as through JEFS as described, *supra*. The parties are reminded that, because the mailing address is not the physical address of this office, some additional screening time is baked into the process. That said, any evidentiary exhibits timely received electronically will be considered timely. The evidentiary exhibits should be mailed to the Hearing Clerk’s address, as follows:

DEA Headquarters
Attn: Hearing Clerk, Office of Administrative Law Judges
8701 Morrisette Drive
Springfield, Virginia 22152

⁵ Exclusive of audio/video recordings, exhibits provided in the form of compact disc (CD), PowerPoints, or other electronic versions will not be accepted, unless otherwise stated in this order or a subsequent one issued by the tribunal.

- All proposed hardcopy documentary exhibits must be supplied in a single-sided format and in an appropriately-sized three-ring binder.
- The electronic version of submitted evidentiary exhibits and the hardcopy binder must also include a Table of Contents listing the number of each proposed exhibit, a brief description of each proposed exhibit, and the number of pages in the proposed exhibit.

Proposed exhibits received after the **January 3, 2025** date fixed in this order for the service and exchange of documents (excluding exhibits to be utilized for cross-examination, rebuttal, and surrebuttal) may not (and likely will not) be admitted into evidence, absent a showing of good cause.

Each party should ensure that it has its own copy of all proposed exhibits for its own use during the hearing.⁶ Further, the parties must ensure that prior to any approved video teleconference testimony, each witness has been furnished with a useable copy (hard copy or otherwise) of any and all proposed exhibits (appropriately marked for identification) that may pertain to that witness's testimony.

IV. Hearing

Under the regulations,⁷ the notice of hearing fixes the place and time for hearing commencement.⁸ In this matter, the GNoH fixed the place of hearing at the DEA Hearing Facility in Arlington, Virginia. 89 Fed. Reg. at 70148-49. As discussed, *supra*, the DEA Hearing Facility will remain the venue throughout the hearing proceedings.⁹

In accordance with 5 U.S.C. § 554(b), the parties were consulted to ascertain the availability of their respective representatives and witnesses. Any party scheduled to present a witness must be present in the courtroom on that date, even if his/her/its witness will be appearing via VTC. Similarly, any representative seeking to cross-examine an opposing witness must likewise be present in the courtroom. Failure to appear, in the absence of good cause and granted by the tribunal in advance, will result in forfeiture of the opportunity to present a witness as well as the opportunity to cross.

⁶ The copies of the documents and/or affidavits exchanged by the parties ahead of the hearing are to serve as opposing parties' working copy during the hearing.

⁷ 21 C.F.R. § 1316.53.

⁸ As directed by the GNoH, the Preliminary Hearing commenced hearing proceedings on December 2, 2024. 89 Fed. Reg. at 70148-49.

⁹ As a reminder, no cell phone use in the courtroom will be permitted throughout the proceedings. No exceptions.

Accordingly, the hearing will commence on **January 21, 2025** at the DEA Hearing Facility. Proceedings will begin at **9:30 a.m. ET** each day and continue through **5:00 p.m. ET** daily from Tuesday through Thursday of each week. There will be a week-long recess from **February 11, 2025** through **February 13, 2025**. The table *infra* outlines the duration of the hearing on the merits in this case:

Week	Activity
1/21/2025—1/23/2025	Hearing
1/28/2025—1/30/2025	Hearing
2/4/2025—2/6/2025	Hearing
2/11/2025—2/13/2025	Break—No Hearing Proceedings
2/18/2025—2/20/2025	Hearing
2/25/2025—2/27/2025	Hearing
3/4/2025—3/6/2025	Hearing

Based on the representations of the parties regarding their representative and witness availability during the Preliminary Hearing, the parties will present their cases in the following order and on the following days:

Presentation Date	Party Name
1/21/2025	Government
1/22/2025	Hemp for Victory (HFV)
1/23/2025	Cannabis Bioscience International Holdings (CBIH)
1/28/2025	Connecticut Office of the Cannabis Ombudsman (OCO); Ellen Brown; and The DocApp (collectively, OCO. <i>et al.</i>)
1/29/2025	National Cannabis Industry Association (NCIA)
1/30/2025	Village Farms International (VFI)
2/4/2025	The Commonwealth Project (TCP)
2/5/2025	Veterans Initiative 22 (VI22)

2/6/2025	Dr. Ari Kirshenbaum
2/18/2025	Tennessee Bureau of Investigation (TBI)
2/19/2025	International Association of Chiefs of Police (IACP)
2/20/2025	Drug Enforcement Association of Federal Narcotics Agents (DEAFNA)
2/25/2025	Smart Approaches to Marijuana (SAM) and State of Nebraska (NE) (collectively, SAM, <i>et al.</i>)
2/26/2025	Community Anti-Drug Coalitions of America (CADCA)
2/27/2025	Cannabis Industry Victims Educating Litigators (CIVEL)
3/4/2025	Dr. Kenneth Finn
3/5/2025	National Drug and Alcohol Screening Association (NDASA)
3/6/2025	Dr. Phillip Drum

Pursuant to 21 C.F.R. § 1316.44 and 21 C.F.R. § 1316.53, regulatory provisions requiring publication of the time and place of the hearing in the Federal Register are waived.

V. Subpoenas

The parties are advised that any requests for subpoenas¹⁰ are to be filed no later than **The Homework Date**. Each subpoena shall be completed in advance by the party seeking it, and the completed subpoena shall be filed with this tribunal with a request for issuance.¹¹ As explained during the Preliminary Hearing, the authority of a DEA ALJ's subpoena authority extends only

¹⁰ 21 C.F.R. § 1316.52(d).

¹¹ To the extent that either party seeks to present witness testimony through VTC, the following language should be utilized to compel testimony by virtual attendance in a subpoena: "At the Drug Enforcement Administration Hearing Facility, located at 700 Army Navy Drive, 2nd Floor, Arlington, Virginia, 22202, by **VIRTUAL APPEARANCE** through a link to be furnished by the requesting party n/l/t one (1) day prior to the date and time of your scheduled appearance and testimony. The testimony will be recorded verbatim through a reporting company under contract with the United States Government."

as far as “to the extent necessary to conduct [the] administrative hearing[] pending before him.” 21 C.F.R. § 1316.52(d).

The subpoena template may be found on the Office of Administrative Law Judges’ website at <https://www.dea.gov/administrative-law-judges>. Subpoena requests that do not comply with these instructions will be returned to the requestor without further action. The party seeking to secure evidence through the use of a subpoena will be responsible for ensuring proper service.

VI. Motions

In view of the robust level of motion practice that has accompanied prehearing proceedings, as announced at the Preliminary Hearing, the time for seeking relief through motion practice has reasonably passed. The time has come to receive evidence and proceed with the hearing. Any further motions must be accompanied by a request to file out of time and supported by a demonstration of good cause that is likely to be narrowly construed.

VII. E-Filing

All proceedings will be governed by the provisions of 21 C.F.R. §§ 1316.41-1316.68.¹² The parties’ attention is specifically directed to 21 C.F.R. § 1316.45, which provides, *inter alia*, that “[d]ocuments shall be dated and deemed filed upon receipt by the Hearing Clerk.” In these formal rulemaking proceedings, documents (other than proposed evidentiary exhibits) must be filed electronically. The exclusive method of filing correspondence in these proceedings is as a PDF attachment via email to the DEA Judicial Mailbox (ECF-DEA@dea.gov). The forwarding email on all electronically-filed correspondence must indicate that it was simultaneously served on the opposing parties via email. The Designated Participants must ensure that all documents filed with the DEA Judicial Mailbox are simultaneously served on the Government Mailbox at (dea.registration.litigation@dea.gov). Any request(s) to modify email addresses of a party or counsel must be made on notice to this tribunal and the parties. The email receipt date reflected by the DEA Judicial Mailbox server shall conclusively control all issues related to the date of service of all filed correspondence, provided however, that correspondence received after 5:00

¹² Additional helpful information regarding DEA administrative proceedings may be found at the OALJ website, <https://www.dea.gov/administrative-law-judges>.

p.m., local Washington, D.C. time, will be deemed to have been received on the following business day. ***Note: While email is utilized as the method to forward documents for filing—as attachments—no substantive matter communicated through the body of a forwarding email will be considered.*** The parties are directed to refrain from including social security numbers or personally identifiable information in electronically-filed documents. ***Proposed exhibits will not be accepted via electronic filing, but must be filed in hard copy and through JEFS as detailed, supra.***

Dated: December 4, 2024

JOHN

MULROONEY

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JOHN MULROONEY

Date: 2024.12.04

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JOHN J. MULROONEY, II
Chief Administrative Law Judge

CERTIFICATE OF SERVICE

This is to certify that the undersigned, on December 4, 2024, caused a copy of the foregoing to be delivered to the following recipients: (1) Julie L. Hamilton, Esq., Counsel for the Government, via email at julie.l.hamilton@dea.gov; James J. Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; Jarrett T. Lonich, Esq., Counsel for the Government, via email at jarrett.t.lonich@dea.gov; and S. Taylor Johnston, Esq., Counsel for the Government, via email at stephen.t.johnston@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington, Esq., Counsel for Village Farms International, via email at spennington@porterwright.com; and Tristan Cavanaugh, Esq., Counsel for Village Farms International, via email at tcavanaugh@porterwright.com; (4) Nikolas S. Komyati, Esq., Counsel for National Cannabis Industry Association, via email at nkomyati@foxrothschild.com; William Bogot, Esq., Counsel for National Cannabis Industry Association, via email at wbogot@foxrothschild.com; and Khurshid Khoja, Esq., Counsel for National Cannabis Industry Association, via email at khurshid@greenbridgelaw.com; (5) Dante Picazo for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (6) Andrew J. Kline, Esq., Counsel for Hemp for Victory, via email at AKline@perkinscoie.com; and Abdul Kallon, Esq., Counsel for Hemp for Victory, via email at and AKallon@perkinscoie.com; (7) Timothy Swain, Esq., Counsel for Veterans Initiative 22, via email at t.swain@vicentellp.com; Shawn Hauser, Esq., Counsel for Veterans Initiative 22, via email at s.hauser@vicentellp.com; and Scheril Murray Powell, Esq., Counsel for Veteran's Initiative 22, via email at smpesquire@outlook.com; (8) Kelly Fair, Esq., Counsel for The Commonwealth Project, via email at Kelly.Fair@dentons.com; (9) Rafe Petersen, Esq., Counsel for Ari Kirshenbaum, via email at Rafe.Petersen@hklaw.com; (10) David G. Evans, Esq., Counsel for Cannabis Industry Victims Educating Litigators, Community Anti-Drug Coalitions of America, Phillip Drum,

Kenneth Finn, International Academy on the Science and Impacts of Cannabis, and National Drug and Alcohol Screening Association, via email at thinkon908@aol.com; (11) Patrick Philbin, Esq., Counsel for Smart Approaches to Marijuana, via email at pphilbin@torridonlaw.com; and Chase Harrington, Esq., Counsel for Smart Approaches to Marijuana, via email at charrington@torridonlaw.com; (12) Eric Hamilton, Esq., Counsel for the State of Nebraska, via email at eric.hamilton@nebraska.gov; and Zachary Viglianco, Esq., for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (13) Gene Voegtlin for International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (14) Gregory J. Cherundolo for Drug Enforcement Association of Federal Narcotics Agents, via email at executive.director@afna.org and afna.org@gmail.com; (15) Reed N. Smith, Esq., Counsel for the Tennessee Bureau of Investigation, via email at Reed.Smith@ag.tn.gov; and Jacob Durst, Esq., Counsel for Tennessee Bureau of Investigation, via email at Jacob.Durst@ag.tn.gov; and (16) Matthew Zorn, Esq., Counsel for OCO et al, via email at mzorn@yettercoleman.com.

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Office of Administrative Law Judges

UNITED STATES DEPARTMENT OF JUSTICE

Drug Enforcement Administration

In the Matter of

**Schedules of Controlled Substances:
Proposed Rescheduling of Marijuana**

**DEA Docket No. 1362
Hearing Docket No. 24-44**

**ORDER REGARDING VILLAGE FARMS INTERNATIONAL,
HEMP FOR VICTORY, AND OCO, ET AL.'S MOTION TO RECONSIDER**

On January 6, 2025, Village Farms International, Hemp for Victory, and OCO, *et al.* (collectively, the Movants), filed a motion (Motion to Reconsider or MTR) seeking, *inter alia*, reconsideration of tribunal's November 27, 2024 order (*Ex Parte* Order or EPO) regarding alleged *ex parte* communications related to the above-captioned matter.¹ MTR at 5-7, 40-43. The Government timely filed its opposition (Opposition).

When assessing a motion to reconsider interlocutory decisions that are not case dispositive, a trier of fact must assess whether there has been a clear error of law, newly discovered evidence,² or a need to prevent manifest injustice. *Intera Corp. v. Henderson*, 428 F.3d 605, 620 (6th Cir. 2005), *cert. denied*, 547 U.S. 1070 (2006); *Firestone v. Firestone*, 76 F.3d 1205, 1208 (D.C. Cir. 1996); *EEOC v. Lockheed Martin Corp.*, 116 F.3d 110, 112 (4th Cir. 1997); *Virgin Atlantic Airways, Ltd. v. National Mediation Board*, 956 F.2d 1245, 1255 (2d Cir. 1992), *cert. denied*, 506 U.S. 820 (1992).

Accordingly, inasmuch as the Movants' Motion to Reconsider sufficiently establishes none of these regulatory prerequisites, it is herein **DENIED**.

In its MTR, the Movants have requested that in the event the relief they seek is denied, that they be granted leave to file an interlocutory appeal. MTR at 43. Under the DEA

¹ The MTR also seeks preemptive summary exclusion of one of the Government's proposed exhibits. MTR at 27. This issue will be reserved if/until the document is offered into the record.

² Any evidence purported to be newly discovered, even to the extent conceded as accurate, would not change the analysis or result in the EPO. That said, I will assume without deciding that the discovery of these new factual bases upon which to seek relief constitute at least sufficient cause to support the Movants' petition to file out of time based on new evidence. Accordingly, that aspect of the Movants' motion is herein **GRANTED**.

regulations, in most circumstances, an interlocutory appeal requires the consent of the presiding administrative law judge. 21 C.F.R. § 1316.62. Specifically, consent requires my certification that such an interlocutory review “is clearly necessary to prevent exceptional delay, expense or prejudice to any party, or substantial detriment to the public interest.”³ *Id.* As discussed in the EPO, the Movants have not met their burden on the issue of whether an *ex parte* hearing should be conducted,⁴ and to the extent that they seek an order from me relieving the Administrator from her proper procedural role as the proponent of the notice of proposed rulemaking (NPRM),

³ There is no specific regulatory requirement that I find that the attendant legal issues are not specious, or that they constitute a sound litigation strategy.

⁴ Inasmuch as the factual underpinnings of the EPM and the MTR have been assumed as accurate for the purposes of a disposition of this issue, an extensive hearing on the issue would serve no purpose. Further, the cases the Movants principally rely upon involve inapplicable facts. In *Professional Air Traffic Controllers Organization (PATCO) v. Federal Labor Relations Authority (FLRA)*, 672 F.2d 109, 110-11 (D.C. Cir. 1982) (*PATCO I*) and *PATCO v. FLRA*, 685 F.2d 547, 574-75 (D.C. Cir. 1982) (*PATCO II*), the court addressed allegations that actual decisionmakers in the process had participated in *ex parte* communications. There are no like allegations in the attendant proceedings. In *PATCO II*, the court held that no disturbance of the agency’s decision was warranted because no taint to the ultimate decision was demonstrated. *PATCO II*, 685 F.2d at 575. The *PATCO II* court conceded that the agency’s “handling of the case has [not] been a paragon of administrative procedure,” but affirmed the decision notwithstanding. *Id.* at 574. The provision of the Administrative Procedure Act (APA) (5 U.S.C. § 556(b)) relied upon by the Movants pertains to challenges raising “personal bias or other disqualification of a[n ALJ] or participating employee.” MTR at 4-5. There has been no allegation related to me or to any employee to be tasked with deciding the case or participating in that decision. Accordingly, this provision appears to be inapposite. Further, in contrast to *ex parte* communication claims, any claims founded exclusively on the DEA’s continuing work with advocacy groups, such as the Community Anti-Drug Coalitions of America (CADCA) or Smart Approaches to Marijuana (SAM), whether recently or in the past, are wholly unpersuasive. The DEA has worked with a multitude of citizens groups over the years in furtherance of its public safety mission, and to disqualify any of these groups would be as ill-advised as precluding participation by those who have advocated before the Agency (formally and/or informally) for a change in marijuana laws.

they have requested relief well beyond my authority to grant.⁵ The original *Ex Parte Motion* (*Ex Parte Motion* or EPM) allegations (as well as some new ones raised in the MTR), even if

⁵ These issues were exhaustively addressed in the *Ex Parte* Order. While the APA and the implementing regulations to the Controlled Substances Act (CSA) supply adequate authority to manage active litigation and prehearing proceedings, an administrative law judge's authority is not inherent, not unlimited, and must be strictly cabined by the parameters of those sources. In their Motion to Reconsider, the Movants argue the issue of ALJ authority on two planes. The first, is purportedly to *enlighten* the tribunal that it has (and always had) authority to conduct an inquiry on alleged *ex parte* communications. MTR at 26. This argument would possess increased gravitas had it not been the case that the EPO, citing the relevant provisions of the APA, actively analyzed and considered the allegations in full. The (still correct) EPO held that even if these communications were assumed as true, they would have no impact on how the case will be decided. EPO at 7 (*citing Raz Inland Navigation Co., Inc. v. ICC*, 625 F.2d 258, 260-62 (9th Cir. 1980)). *Ex parte* communications do not void an agency decision, but make it voidable if the "agency's decisionmaking process [is] irrevocably tainted so as to make the ultimate judgment of the agency unfair, either to an innocent party or to the public interest that the agency [is] obliged to protect." *PATCO II*, 685 F.2d at 564. The MTR raises additional (admittedly equally appalling) allegations of *ex parte* communication to one side of the litigation equation by at least one high-level Agency official to an anti-NPRM entity, in an apparent effort by the former to enhance to latter's chance of selection as a designated participant above others who applied. This arguably disturbing and embarrassing revelation, even credited, still does not demonstrate an "irrevocable taint" that will affect the ultimate outcome of the proceedings. This is keenly so where the Movants have alleged that the DEA came to the table possessed of an "unalterably closed mind." MTR at 4, 40. If the Agency's mind was indeed "unalterably closed," it is difficult to imagine that any of the comments of Dr. Sabet would have changed that, or that the Agency would not have included the Tennessee Bureau of Investigation (TBI), even without revisions to its application. Foolishness does not always result in cognizable prejudice, and it has not done (and will not do) so here. I stand unaffected (and certainly unimpressed) by the Agency's actions in this regard, and in light of the results of the recent presidential election and the imminent replacement of the current Administrator (*see n.5, infra*), these developments (whether newly-discovered or otherwise) are unlikely to affect the outcome of these proceedings. The second plane persists in its insistence that the tribunal possesses the authority to remove the DEA Administrator (that is, the DEA Administrator who is soon to be replaced by the new administration and who assigned the ALJ to adjudicate this matter) from her role as the proponent of (and presumably in adjudicating) the NPRM. MTR at 39-41. This theory stands as unsupported and strange now as it did when first proposed in the EPM. I can no more remove or re-designate the Administrator than I can hold parties in contempt and fine them. The strangeness of this unsupported approach is amplified by the fact that the appointment of a new DEA Administrator by a different political party is imminent. Similarly, the concept that the Movants are somehow entitled to an agency head who is steadfastly convinced of the correctness of their position before the first witness has been sworn, is as peculiar as their insistence that the ALJ assigned to the case has some bizarre, inherent authority to remove the head of the Agency from its place as the proponent of the NPRM. In this regard, the MTR speaks without authority or common sense. If this aspect of the relief it seeks were to be (erroneously) granted, the results would be: (1) certain (correct), swift reversal by the Agency or the courts; and (2) a conversion of the proceedings from a timely, legally-correct hearing to a circus that would add nothing to the rescheduling cause the Movants purportedly espouse. The Movants are not entitled to a perpetual cheerleader-proponent who is forbidden from maintaining or evolving her position, and the public would arguably be ill-served by having one. Even to the extent that the (current) Administrator holds some reservations as to whether the proposed rescheduling adequately discharges her responsibilities under the CSA, the APA is unequivocal that "the proponent of a rule ... has the burden of proof." 5 U.S.C. § 556(d). The Movants can (and should) avail themselves of the opportunity to present their best case to shoulder that burden. Even if the Agency has not noticed (and does not present) the quality and quantum of evidence the Movants subjectively believe it should, there is nothing preventing the Movants from doing so, compiling an unimpeachable record of proceedings, and prevailing. It is not the number of Designated Participants (DPs) that will carry the day, but the strength of the arguments and evidence presented. A contrary result could engender a perpetual evaluation of the strength and precision of the Agency's case throughout the proceedings, with the potential for reconsideration motions at every turn where the Movants find the skill of the Government's counsel wanting. Opposing sides of a litigation equation do not stand in the position of evaluating and critiquing the quality of the other side's case. That is my function and the function of those in the Agency and the courts who review my recommended decision. An evidentiary hearing does not lend itself well to an academic

conceded as having some factual basis, while unseemly and troubling,⁶ would not (and will not) affect the outcome of this action.⁷

Notwithstanding the pleas of the Designated Participants that they are anxious for action on the proposed rescheduling of marijuana, the Movants (a subset of the pro-rescheduling DPs) are apparently eager to trade a timely disposition and recommended decision⁸ for the dubious advantage of piling on more DPs.

experiment where intellectually novel and curious issues are created and tested, just for the sake of doing so. This is particularly true here, where the American public and the true proponents and antagonists have waited so long, prepared their cases, and cleared their calendars.

⁶ To be sure, the specter of officials at the highest level of Agency management selectively assisting and granting access to individuals and groups standing in opposition to the NPRM it purportedly supports as the proponent, carries no small measure of discomfiture. If true, viewed in the best light, these allegations demonstrate a puzzling and grotesque lack of understanding and poor judgment from high-level officials at a major federal agency with a wealth of prior experience with the APA. And that is a charitable perspective. But as discussed in the EPO, the true issue is not discomfiture, but whether the quality of the prior conduct of one or more of the Agency's functionaries will affect the outcome of the proceedings. I am certainly not influenced in any way helpful to the Government by these allegations, and the DPs have not been inhibited in their ability to produce the most persuasive evidence at their disposal (even including written materials or testimony from those whom the Administrator did not designate). Even beyond that, as discussed, *infra*, the appointment of a new DEA Administrator is imminent. In short, there is practically zero chance that the allegations, even if established by the requisite standard, would affect the fairness of the adjudication of the NPRM (whether that decision is ultimately for or against its promulgation). That is not to say that continued misadventures will come without consequences (now or on review by the courts), but on the present record, I have determined that the outcome of the proceedings will not be adversely affected by the facts as alleged in the EPM or the MTR. Stated differently, nothing in this order or the EPO should be read to countenance continued unwise, risky, or careless behavior on the part of the Government. Similarly, the Government should take heed that, to the extent that it becomes apparent that the actions of the Agency have "irrevocably tainted" the proceedings, this tribunal is not without viable options that actually are authorized under the law. *PATCO II*, 685 F.2d at 564-65. For example, there is nothing in the CSA, the APA, or the regulations that would preclude this tribunal from terminating hearing proceedings and transmitting a decision recommending a restart to the entire process and the issuance of a new NPRM. There are other draconian procedural options available as well. Stated differently, the conclusion that an irrevocable taint has not been demonstrated by the Movants is not coextensive with the conclusion that a duly-appointed ALJ is relegated to standing by as a passive observer without the ability to act. The Movants here have neither established the requisite level of cognizable prejudice to the ultimate outcome, nor sought a realistic remedy. By the same token, the Government's failure to acknowledge in any way the gravity of the highest levels of its organization allegedly reaching out to help one of the potential DPs fortify its application to ease the task of justifying its apparently pre-made determination for appeal (Opp. at 8) demonstrates an arrogant overconfidence that may not serve it well in the future. Likewise, the Government's dismissive assertion that all procedural anomalies, irrespective of severity or collective impact, should be directed to the appellate courts (Opp. at 10) suffers from the same defect. These are formal hearing proceedings, not a deposition.

⁷ The Administrative Procedure Act and the DEA regulations authorize the identification, recognition and inclusion of material facts in the administrative record by the taking of official notice. 5 U.S.C. § 556(e); *Attorney General's Manual on the Administrative Procedure Act* 80 (1947); 21 C.F.R. § 1316.59(e). Accordingly, official notice is herein taken that in November 2024, a new president from a different political party was elected, and the new president is scheduled to be inaugurated on January 20, 2025. Official notice is also taken that the current Administrator has publicly signaled her intention to depart the Agency prior to the inauguration of the new president. To the extent either party seeks to challenge the factual predicate of the official notice taken in this matter it may file an appropriate motion no later than fifteen (15) days from the issuance of this order.

⁸ Even an adverse decision efficiently rendered would move the ball forward.

Even factoring in the reality that sometimes litigants and their representatives should be mindful of what they wish for,⁹ to the extent my analysis is found to be in error on review, I am willing to certify that the allowance of this interlocutory appeal could potentially avoid exceptional delay, expense or prejudice to the DPs and the Government by injecting appellate certainty into the equation at this stage of proceedings. Were my analysis to be reviewed on appeal and determined to constitute prejudicial error, a remand would clearly result in significant delay and expense to the Designated Participants and the process.

Accordingly, that aspect of the Movants' Motion to Reconsider that seeks leave to file an interlocutory appeal is **GRANTED**, the hearing on the merits that was scheduled to commence on January 21, 2025 is **CANCELLED**, and proceedings in this matter are **STAYED**, pending a resolution of the interlocutory appeal to the DEA Administrator.¹⁰

It is further **ORDERED** that the Movants and the Government provide this tribunal with a joint status update ninety (90) days from the issuance of this order, and every ninety (90) days thereafter. Either the Movants or the Government may file the status update, but one party must file one.

It is further **ORDERED** that a briefing schedule will be fixed by the Office of the Administrator, but all correspondence related to the interlocutory appeal will travel through the

⁹ As must have been anticipated by the Movants, an interlocutory appeal returns jurisdiction of the matter to the full control of DEA Agency leadership in all respects. 21 C.F.R. § 1316.62. The matter is on stay here, and the Administrator will issue a briefing schedule, entertain oral argument if he/she desires, and issue a binding, written decision on this tribunal. *Id.* It may be worth considering, however, that in this case, notwithstanding the plain language of the regulations, that the definition of an "interested person" includes only "any person *adversely affected or aggrieved* by any rule or proposed rule issuable pursuant to [21 U.S.C. § 811]" (21 C.F.R. § 1300.01 (emphasis supplied)), the Standing Order (currently law of the case) balanced a significant level of federal precedent to render a more nuanced, four-factor view that included persons who actually support the NPRM. That is, persons are currently included in the litigation that have alleged neither adverse affect nor aggrievement by NPRM. Stated differently, an interpretation that applies the plain language of the regulation and excludes supporters of the proposed rescheduling is certainly a perfectly defensible (and some might argue, advisable) legal position for the Agency to embrace or evolve to. Even now. Naturally, this would be likewise true about an Agency decision to restart or even withdraw the NPRM. Ironically, had the Administrator elected at the outset to narrow the scope of participants within the strict parameters of the regulations (that is, to limit inclusion to only those adversely affected or aggrieved), without any of the unpalatable noise associated with the alleged *ex parte* communications, it is likely that such decision would have been easily sustained on review and the Movants would not have the voice they currently enjoy in these proceedings. Thus, the Administrator's election to extend a participation invitation beyond the parameters of the regulation (a decision which is not subject to my review) could conceivably be viewed as an act of administrative grace aimed at an increased level of inclusivity, but hardly an irreversible one.

¹⁰ While the Movants contemplate that an affidavit they intend to file will be reviewed by both the DEA and the DOJ (MTR at 5, 41, 44) they have supplied no authority or mechanism that would authorize any action beyond a review by the DEA Administrator. 21 C.F.R. § 1316.62. In short, there is no indication of how the Movants expect any affidavit or review would ever be tendered to the Attorney General.

DEA Judicial Mailbox to be forwarded to that office.

Dated: January 13, 2025

**JOHN
MULROONEY**
JOHN J. MULROONEY, II
Chief Administrative Law Judge

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CERTIFICATE OF SERVICE

This is to certify that the undersigned, on January 13, 2025, caused a copy of the foregoing to be delivered to the following recipients: (1) Julie L. Hamilton, Esq., Counsel for the Government, via email at julie.l.hamilton@dea.gov; James J. Schwartz, Esq., Counsel for the Government, via email at james.j.schwartz@dea.gov; Jarrett T. Lonich, Esq., Counsel for the Government, via email at jarrett.t.lonich@dea.gov; and S. Taylor Johnston, Esq., Counsel for the Government, via email at stephen.t.johnston@dea.gov; (2) the DEA Government Mailbox, via email at dea.registration.litigation@dea.gov; (3) Shane Pennington, Esq., Counsel for Village Farms International, via email at spennington@porterwright.com; and Tristan Cavanaugh, Esq., Counsel for Village Farms International, via email at tcavanaugh@porterwright.com; (4) Nikolas S. Komyati, Esq., Counsel for National Cannabis Industry Association, via email at nkomyati@foxrothschild.com; William Bogot, Esq., Counsel for National Cannabis Industry Association, via email at wbogot@foxrothschild.com; and Khurshid Khoja, Esq., Counsel for National Cannabis Industry Association, via email at khurshid@greenbridgelaw.com; (5) Dante Picazo for Cannabis Bioscience International Holdings, via email at ir@cbih.net; (6) Andrew J. Kline, Esq., Counsel for Hemp for Victory, via email at AKline@perkinscoie.com; and Abdul Kallon, Esq., Counsel for Hemp for Victory, via email at AKallon@perkinscoie.com; (7) Timothy Swain, Esq., Counsel for Veterans Initiative 22, via email at t.swain@vicentellp.com; Shawn Hauser, Esq., Counsel for Veterans Initiative 22, via email at s.hauser@vicentellp.com; and Scheril Murray Powell, Esq., Counsel for Veteran's Initiative 22, via email at smpesquire@outlook.com; (8) Kelly Fair, Esq., Counsel for The Commonwealth Project, via email at Kelly.Fair@dentons.com; Joanne Caceres, Esq., Counsel for The Commonwealth Project, via email at joanne.caceres@dentons.com; and Lauren M. Estevez, Esq., Counsel for The Commonwealth Project, via email at lauren.estevez@dentons.com; (9) Rafe Petersen, Esq., Counsel for Ari Kirshenbaum, via email at Rafe.Petersen@hklaw.com; (10) David G. Evans, Esq., Counsel for Cannabis Industry Victims Educating Litigators, Community Anti-Drug Coalitions of America, Kenneth Finn, International Academy on the Science and Impacts of Cannabis, and National Drug and Alcohol Screening Association, via email at thinkon908@aol.com; (11) Patrick Philbin, Esq., Counsel for Smart Approaches to Marijuana, via email at pphilbin@torridonlaw.com; and Chase Harrington, Esq., Counsel for Smart Approaches to Marijuana, via email at charrington@torridonlaw.com; (12) Eric Hamilton, Esq., Counsel for the State of Nebraska, via email at eric.hamilton@nebraska.gov; and Zachary Viglianco, Esq., for the State of Nebraska, via email at zachary.viglianco@nebraska.gov; (13) Gene Voegtlin for International Association of Chiefs of Police, via email at voegtlin@theiacp.org; (14) Patrick Kenneally, Esq. Counsel for Drug Enforcement Association

of Federal Narcotics Agents, via email at pdkenneally78@gmail.com; (15) Reed N. Smith, Esq., Counsel for the Tennessee Bureau of Investigation, via email at Reed.Smith@ag.tn.gov; and Jacob Durst, Esq., Counsel for Tennessee Bureau of Investigation, via email at Jacob.Durst@ag.tn.gov; and (16) Matthew Zorn, Esq., Counsel for OCO *et al.*, via email at mzorn@yettercoleman.com.

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Secretary (CTR)
Office of Administrative Law Judges

**AFNA**Association of Federal Narcotics Agents
www.afna.orgDrug Enforcement Administration
Attn: Honorable Anne Milgram
8701 Morrisette Drive
Springfield, VA 22152

February 28, 2024

Honorable Anne Milgram-

As President of the DEAFNA (Drug Enforcement Association of Federal Narcotics Agents), I am writing to urge the current Administration not to knowingly fail this country's youth by rescheduling marijuana from the current and justified Schedule I classification.

Recent communication from the Assistant Secretary for Health and Human Services (HHS) in support of rescheduling marijuana is unfounded and *in direct contradiction* with its own SAMHSA (Substance Abuse and Mental Health Services Administration) evidence-based literature, NSDUH (National Survey on Drug Use and Health) reports, and grantee marijuana attestation requirements.

Numerous independent studies exist which quantify the steep rise in incidence of addiction, psychosis and mental illness directly resulting from increased marijuana use, especially among adolescents. The nexus between chronic use and mental illness is proven to increase homelessness effecting children and veterans the most. Related increases have been well-documented in marijuana-impaired driving incidents, emergency room visits, and hospitalizations. The negative impact of marijuana is undeniable and, in many cases, *permanent*. Even HHS's own NIDA (National Institute on Drug Abuse) continues to publish studies warning about the significant harmful effects of teen marijuana use including permanent IQ reduction and schizophrenia. Administration support of marijuana rescheduling sends a clear message to our country's youth that risky behavior is condoned, and mental wellness is disregarded.

Lastly, there has been no scientific evidence brought forward to support a new ruling for marijuana based on the eight factors determinative of control or removal from schedules contained in 21 U.S. Code § 811(c) or 21 U.S. Code § 812(b)(1).

DEAFNA is comprised of retired and active DEA agents, who unquestionably understand this issue from every perspective. In fact, DEA agents are the only federal employees whose sole mission since 1973 has been to enforce the controlled substances laws and regulations of the United States.

We are adamantly opposed to any intentional move that we predict will have such a drastically negative and permanent impact on public safety and health. I am attaching a position paper authored by two of our members that addresses our concerns in greater detail.

Thank you for your consideration of our request.

Sincerely,

Marshall Fisher
PresidentDrug Enforcement Association of Federal Narcotics Agents (DEAFNA)
marshallfisher@rocketmail.com

For the first time in history, to our recollection, the Regulatory and Scientific process has been subverted by the political process in scheduling of a controlled substance and the integrity of the U.S. prescription drug market is at substantial risk. The Biden administration and the members of congress believe rescheduling marijuana will draw votes and lead to a miracle cures. In fact, this movement is driven by a well-funded lobby effort which is putting dollars and revenue above public health and safety. This is the same playbook used by special interest groups with tobacco and many of the same special interest groups involved with tobacco are now involved with the marijuana lobby.

Science and evidence – not public opinion or ideology – should drive public health and policy in America. In many States that voted for medical and recreational marijuana legalization, we are now seeing evidence of regret after the increase of marijuana shops and advertising in communities. The promises of a huge financial windfall and the crippling of the underground economy for marijuana have not manifested, instead, the black market for marijuana is proliferating. In Colorado, California, and Oregon, most towns, when given a choice, have rejected having “pot” shops in their communities at the polls.

In our opinion, HHS made the political decision to only focus on data which supports the rescheduling of marijuana; thereby, making a disingenuous argument the Federal government should consider this effort due to a political promises; most of the public would not agree with unless the survey questioning was loaded to answer in the affirmative. The FDA threw out the scientific five fact analysis to determine if marijuana has any currently accepted medical use. In order to reach their predetermined outcome HHS changed the criteria at the detriment of the future of our citizens and their health and safety. Why would FDA now deviate from using this five-factor test and rely on state ballot votes in the determination that marijuana has accepted medical use? This standard has never before been used to determine if a so-called medicine is safe for the public.

In our analysis we found, none of the studies used by FDA justify the claim that marijuana is medicine. One study results indicated mixed or inconclusive results to what it claimed to cure. Another study had results which were not statistically significant. Yet another study resulted in findings which were insignificant, and also showed increased risks; thereby, limiting the effectiveness of marijuana.

The Five Part Test which FDA ignored consider:

- The drug’s chemistry must be known and reproducible – which marijuana is not unlike other pharmaceutical prescription drugs.
- There must be adequate safety studies – which a recent following of the medical reporting of the link between marijuana use and psychosis and mental illness supports the concept FDA did not fully consider safety.
- There must be adequate and well-controlled studies proving efficacy – which the above three studies used by FDA cut against their own flawed justification.
- The drug must be accepted by qualified experts – the American Psychiatric Association stated – “marijuana is known to worsen certain psychiatric conditions.
- The scientific evidence must be widely available – as stated above we are not sure you can find this type of evidence and you will certainly not have medical experts agree on sufficient data which concludes marijuana is medicine.

The 2016 scheduling review of marijuana concluded that “Marijuana does not meet ANY of the five elements necessary for a drug to have a currently accepted medical use”.....so FDA developed a “two-part” test which is reduced down to the fact that if a doctor or health care practitioner prescribes marijuana under state passage of well-funded industry ballot measures it must have medical use. Nothing has changed since 2016, except marijuana and marijuana products are more widely available due to well-

funded ballot initiatives. The potency and negative impacts upon the U. S. continue to increase and take us further away from being close to being able to meet any of the five elements the FDA must consider.

Consider this https://www.youtube.com/watch?v=KYsWZCf_YMw – we now know this clip to be less than accurately shared information. In 2016 DEA justifications addressed the reasons why medical practitioners were not qualified to evaluate safety and effectiveness of drugs and that health care practitioners did not meet the definition of qualified experts to determine the safety and effectiveness of a drug. We can only deduce that FDA clearly knew they could not pass the five-factor test so it appears the political leadership of the organizations rather than the career professionals who have experience with this, and other drug scheduling efforts developed a modified “two-part” test which would provide FDA with the answer they were seeking. This “two-part” test was created to avoid the standards other drug are held to, due to the insufficient amount of existing research into the safety and efficacy of marijuana as a medicine. Furthermore, a 2023 study indicated that only 10% of physicians who can prescribe medical cannabis authorization forms for their patients authorize and prescribe the use of cannabis products.

As is often cited by the organization Smart Approaches to Marijuana (SAM), scheduling of drugs is not directly used to determine criminal penalties for drugs and scheduling is not synonymous with the danger of a drug. Rather, it is a technical legal term that categorizes drugs according to their potential for abuse and accepted medical value. Marijuana meets the technical definition of Schedule I because it has a high potential for abuse and has no FDA-approval for use in medical treatment in the U.S.

Rescheduling is also a source of major confusion. Rescheduling marijuana – while symbolically important for special interest groups – would not have much of a real-world consequence in terms of reducing criminal penalties. Recreational use of Schedule II drugs is still illegal and can come with significant criminal liability.

SAM published a six-point plan in 2015 that called for changes such as allowing more licensees to grow marijuana for research purposes and establishing compassionate research programs for the seriously ill and DEA has made efforts to do exactly that so there can be real Scientific case studies to support such a move and “legalize” marijuana, however the special interests group realize that given more time the argument for this move will disappear especially given the overwhelming and increasing evidence of the link between marijuana use and mental illness. Within the last several weeks there has been more reporting on the troubling finding link marijuana use to mental illness.
<https://www.wsj.com/articles/marijuana-is-more-dangerous-than-bidens-hhs-lets-on-psychosis-heart-pregnancy-fe409dba>

Also, as pointed out by SAM, there is support to e fast-track the FDA process to extract non-smoked medications from the cannabis plant. In the meantime, before we have more cannabis-based FDA-approved medications, FDA and HHS should administer a program whereby the truly sick and dying can receive yet-to-be approved, non-psychoactive, non-smoked components of marijuana under a special research program. However, rescheduling marijuana is neither necessary nor desirable for those actions to happen. Rescheduling marijuana would do nothing to allow for more cannabis-based medicines. In fact, cocaine is Schedule II today and is not allowed in a widespread fashion. Rescheduling would simply be a symbolic victory for advocates who want to legalize marijuana. If legalization is the end game for this administration, the more appropriate action would be to clearly state their goal to Congress. This current attempt to reschedule marijuana outside the normal protections afforded the public threatens to destroy the process by which all drugs are evaluated for medical use in this country. This would have extreme and potentially deadly consequences to the American public. Also this would action would be to the detriment and integrity of our widely accepted and respected pharmaceutical approval process in the United States, as opposed to putting pressure on the Federal Agency who is empowered with scheduling controlled substances and following the process congress intended for them to follow rather than the one set forward

by this or any administration's political decision making process within HHS, which is in our opinion to the detriment of the United States and its citizens.

While there are many other factors to consider around this decision and the "legalization" and rescheduling of marijuana (safety, health, increases in crime, increases in instances of mental illness/addiction and violations of U.S. international treaties and agreements), as it is a very complex issue, we wanted to focus on why DEA should reject this recommendation from HHS and FDA on the rescheduling of marijuana to Schedule III. The examination and research and scientific case to support the HHS recommendation is just not credible. The Drug Enforcement Association of Federal Narcotics Agents do not support such a blatant and obvious attempt at circumventing the tried-and-true process of approving drugs for the American public.



IASIC
PO Box 4187
Burlington, VT 05406-4187

Drug Enforcement Administration
Attention: Administrator
The Honorable Anne Milgram
U.S. Department of Justice
8701 Morrisette Drive
Springfield, VA 22152

June 1, 2024

Dear Administrator Milgram:

On behalf of the International Academy on the Science and Impact of Cannabis (IASIC), we hereby request a hearing regarding Docket No. DEA-1362, A.G. Order No. 5931-2024, the proposed rescheduling of Cannabis from Schedule I to Schedule III of the Controlled Substances Act. IASIC is a physician-driven organization of international experts on cannabis who are guided by science to provide accurate information to educate the public and guide policy making. The co-signatories of this request constitute the leadership of IASIC—all recognized experts in the United States and internationally.

We have an interest in the proceeding as physicians and concerned citizens of the United States of America who believe that re-scheduling will have immediate and irreparable harm to the public health.

We oppose the removal of cannabis from Schedule I. Our specific objections are:

- 1) The Department of Health and Human Services (HHS) wrongly changed the definition of currently acceptable medical use (CAMU)
- 2) Even under the new definition, cannabis still does not meet the requirements for CAMU
- 3) Proper regulation of cannabis as a schedule 3 drug cannot be achieved while non-medical cannabis commerce is allowed.

Attached is a brief discussion of our objections.

Respectfully Submitted,

Eric A. Voth, MD, FACP
Internal Medicine, Pain, Addiction Medicine
President and Chairman of the Board -IASIC
eavmdtop@aol.com
785-272-5872 Cell upon request

Roneet Lev, MD, FACEP
Drug Policy and Emergency Medicine
Vice-President of IASIC & Former Chief
Medical Officer of the White House ONDCP

Ken Finn, MD
Pain Medicine and Drug Policy
Vice-President of IASIC Past-President of the
American Board of Pain Medicine

Catherine Antley, MD
Treasurer of IASIC
Board certified in Anatomic and Clinical
Pathology and Dermatopathology

Elizabeth Stuyt, MD
Board-certified Addiction Psychiatrist
Secretary of IASIC

Russell Kamer, M.D.
Clinical Associate Professor of Medicine
New York Medical College

Statement of Position

In a letter dated August 29, 2023, the Assistant Secretary of Health recommended that “marijuana, referring to **botanical cannabis**” be moved to schedule 3. Although there are federally regulated cannabinoid products that are medicine,¹ botanical cannabis is not. The crude cannabis products that are sold in state-legal medical dispensaries, and the way they are distributed based on a licensed health care practitioner (LHCP) ‘recommendation’ rather than prescription, bear little resemblance to modern accepted medical practice that requires prescription of specified doses of a purified product of known and standardized composition.²

Since botanical cannabis did not meet previous criteria for currently accepted medical use (CAMU), HHS pretextually changed the definition of CAMU from requiring FDA-approval—or meeting FDA’s core standards—to (1) “widespread current experience with medical use” of the substance in the United States by LHCPs operating in accordance with implemented State-authorized programs; and (2) “some” credible scientific support for a least one of those medical uses.

Even using this broader definition, botanical cannabis fails to meet CAMU criteria.

- (1) “Widespread” implies that the drug is broadly accepted and utilized within the medical community. Nothing can be further from the truth. The HHS argument that 30,000 LHCPs are authorized to recommend the use of marijuana sounds impressive until one considers that this

¹ Cannabinoid products approved for medicinal use: (1) a synthetic THC (dronabinol) and (2) synthetic cannabinoid, nabilone, for treating chemotherapy-associated nausea and vomiting and for stimulating appetite in patients with HIV; (3) cannabidiol for treating 2 rare forms of seizures; (4) cannabidiol plus THC in a 1:1 ratio in 28 countries (not in the US) for treating multiple sclerosis-associated spasticity and neuropathic pain. Potenza MN, Bunt G, Khalsa JH. Addiction Medicine Physicians and Medicinal Cannabinoids. *JAMA Psychiatry*. 2023;80(7):659–660. doi:10.1001/jamapsychiatry.2023.0731

² The world-renowned Cleveland Clinic explained, “Medications are tested for safety and efficacy. They are closely regulated, from production to distribution. They are accurately dosed, down to the milligram. Medical marijuana is none of those things... Products such as vaporizers, edibles, oils, tinctures and patches all lack uniform dosing specificity. The levels of THC or CBD can differ greatly from one dispensary to another or one batch to another.” <https://newsroom.clevelandclinic.org/2019/01/10/why-cleveland-clinic-wont-recommend-medical-marijuana-for-patients>

number represents **fewer than 3% of LHCPs** with prescriptive authority. Further attesting to the fact that only a small minority of LHCPs recommend botanical cannabis, data from Colorado showed that, in 2022, **0.1% of LHCPs were responsible for about 73% of the medical marijuana certifications**. Meanwhile, **98% of eligible LHCP wrote no marijuana certifications**.³ Only a fringe minority of LHCPs believe smoking cannabis is medical treatment.

- (2) “*Some*” scientific support for *one* medical use is a low bar to clear, but even here the HHS analysis fails. They opine that science supports using botanical cannabis for “anorexia related to a medical condition; nausea and vomiting (*e.g.*, chemotherapy-induced); and pain.” The problem is that HHS conflates isolated cannabinoids and crude cannabis products. The scientific evidence for these 3 medical uses comes from rigorous studies of the approved cannabinoid medications previously listed.¹ It does not follow that botanical cannabis—with multiple active chemicals—smoked *ad libitum* will have the same effect as medications with small specified doses of a single active chemical. A case in point is that of nausea and vomiting. While dronabinol has been shown to alleviate symptoms of nausea and vomiting, botanical cannabis can lead to intractable vomiting—Cannabis Hyperemesis Syndrome.⁴ Moreover, safety is a major concern as traffic fatalities, psychosis, suicide, violence, depression, mania, maternal-fetal harms, and addiction have been associated with use of botanical cannabis.⁵

The DEA states it will consider the marijuana-specific controls that would be necessary to meet U.S. obligations under the Single Convention, but ignores the issue of state-legal sales of recreational cannabis. Schedule 3 drugs can only be distributed by prescription by DEA registered practitioners. It follows that recreational cannabis stores would have to be shuttered and procedures for medical dispensaries revamped. These issues need to be addressed prior to a final rule.

³ In Colorado, physicians, dentists and advanced practice providers with prescriptive authority may certify a patient for marijuana. By statute, the Department of Public Health & Environment must report annually the number of providers who made medical marijuana recommendations and the number each provider made. Colorado Medical Marijuana Registry 2022 Annual Report. <https://cdphe.colorado.gov/medical-marijuana-registry-data>

⁴ Riha R, Winchell R, Safo D, Gentges J. Cannabinoid Hyperemesis Encounters After Medical Legalization in Oklahoma. *Cureus*. 2023;15(10):e46465. Published 2023 Oct 4. doi:10.7759/cureus.46465

⁵ Mohiuddin M, Blyth FM, Degenhardt L, et al. General risks of harm with cannabinoids, cannabis, and cannabis-based medicine possibly relevant to patients receiving these for pain management: an overview of systematic reviews. *Pain*. 2021 Jul 1;162:S80-96.



Khurshid Khoja

Principal

Greenbridge Corporate Counsel, P.C.
500 Capitol Mall
Suite 2350
Sacramento, CA 95814
greenbridgelaw.com

June 4, 2024

Drug Enforcement Administration
Attn: Hearing Clerk/OALJ
8701 Morrisette Drive
Springfield, VA 22152

Drug Enforcement Administration
Attn: DEA Federal Register Representative/DPW
8701 Morrisette Drive
Springfield, Virginia 22152

Subject: Request for Hearing and Public Comment in Support of Same

Dear DEA staff:

The undersigned individual Khurshid Khoja hereby requests a hearing in the matter of Docket No. DEA-1362, the DEA's Proposed Rule re Schedules of Controlled Substances: Rescheduling of Marijuana ("Proposed Rule"). As explained further in the comment attached hereto as **Attachment A**, I would be *adversely* affected or aggrieved by the Proposed Rule, and specifically the Drug Enforcement Administration's proposed definition of "Tetrahydrocannabinol" under 21 CFR § 1308.11 offered in the Proposed Rule, which would sweep currently non-scheduled cannabinoids without a formal scheduling action as required under the Controlled Substances Act ("CSA") at 21 USC §811(a). This would potentially contradict the advice that I, other legal counsel and other legally-compliant operators throughout the cannabinoid industries have relied upon in good faith for over two decades. Please note that the attached comment is also intended to satisfy the requirements of 21 CFR § 1316.47, as it states with particularity the objections and issues on which I desire to be heard, and offers a brief summary of my position regarding same.

Thank you for considering my request for a hearing on the subjects covered herein, and in the attached written comment submitted in support of this request. All notices to be sent pursuant to the proceeding should be addressed to:

Khurshid Khoja
c/o Greenbridge Corporate Counsel, P.C.
500 Capitol Mall, Suite 2350
Sacramento, CA 95814

Respectfully yours,

A handwritten signature in blue ink, appearing to read "Khurshid Khoja", written in a cursive style.

Khurshid Khoja



Request for Hearing in Docket No. DEA-1362 and
comment to same
June 4, 2024

Attachment A

Comment in the matter of Docket No. DEA-1362, the DEA's Proposed Rule re Schedules of Controlled Substances: Rescheduling of Marijuana ("Proposed Rule") submitted by Khurshid Khoja

I write in my personal capacity as Principal CEO of Greenbridge Corporate Counsel, P.C., as an attorney working in the legal and regulated cannabinoids industry since 2011, representing numerous clients in California's state-licensed marijuana industry, in the federally-legal hemp industry, as well as clients and advocacy groups engaged in scientific and medical research and development. I am also the former Chair of the National Cannabis Industry Association Board of Directors and its current Cochair for Policy, but my comments should not be taken to represent the views of NCIA (which may or may not submit a similar comment).

I strongly oppose any misapplication of the proposed definition to place all non-scheduled synthetic cannabinoids under *tetrahydrocannabinols* (including, but not limited to, therapeutically beneficial and non-intoxicating cannabinoids like CBD, THCV and THCA). As such, I respectfully ask the DEA to revise the proposed definition of "Tetrahydrocannabinol" under 21 CFR [§ 1308.11](#) offered in the Proposed Rule to address any potential confusion over the definition, and its application to other non-scheduled cannabinoids without a formal scheduling action required under the Controlled Substances Act at [21 USC §811\(a\)](#). I propose the following clarifications:

(30) Tetrahydrocannabinols—7370

(i) Meaning synthetic equivalents of tetrahydrocannabinols ($C_{21}H_{30}O_2$), ~~except as in paragraphs (d)(30)(ii) and (iii) of this section,~~ naturally contained in a plant of the genus Cannabis (cannabis plant), ~~as well as synthetic equivalents of the substances contained in the cannabis plant,~~ or in the resinous extracts of such plant, or ~~synthetic substances,~~ any derivatives, and their isomers with ~~similar chemical structure~~ an identical molecular formula and pharmacological activity ~~to that mimics those substances~~ tetrahydrocannabinols contained in the plant.

(ii) Tetrahydrocannabinols do not include any substance, material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.

(iii) Tetrahydrocannabinols do not include any substance, material, compound, mixture, or preparation that falls within the definition of marijuana set forth in 21 U.S.C. 802(16).



Request for Hearing in Docket No. DEA-1362 and
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(iv) For the sake of clarity, tetrahydrocannabinols do not include cannabidiol, tetrahydrocannabinolic acid, tetrahydrocannabivarin or any other synthetic substance with a different molecular formula and/or exhibiting different pharmacological activity.

* * * * *

My concern is prompted by the DEA's recent pronouncements, which suggest that the DEA may well apply its proposed regulation to lawful non-scheduled synthetically-derived non-intoxicating cannabinoids. In a [letter from Terry Boos](#), Chief of the Drug & Chemical Evaluation Section of Diversion Control Division of the DEA, dated May 13, 2024 Dr. Boos communicated the DEA's statutory interpretation of both 21 U.S.C. § 812, Schedule I(c)(17) of the CSA and Section 7 U.S.C. 1639o of the Agriculture Improvement Act of 2018, Public Law 115–334 (the "2018 Farm Bill"), concluding that "*cannabis-derived THCA does not meet the definition of [federally legal] hemp under the CSA because upon conversion for identification purposes as required by Congress, it is equivalent to delta-9-THC,*" and "[t]he CSA classifies tetrahydrocannabinols (*such as THCA*) as controlled in schedule I" (emphasis added). Respectfully, this would be contrary to Congress' intent in scheduling THC, and settled law per valid federal Circuit Court precedents.

Federal appellate precedents established prior to the 2018 Farm Bill are instructive on this point as they have addressed previous attempts by the DEA to expand the definition of "tetrahydrocannabinol," and are still valid law¹ notwithstanding the passage of the 2018 Farm Bill. In *Hemp Industries Association v. DEA*, a trade association representing numerous manufacturers and importers of non-psychoactive hemp foodstuffs challenged DEA Final Rules which sought to expand the definition of "Tetrahydrocannabinols" to include any naturally occurring THC regardless of whether such THC is derived from marihuana or hemp (which was more narrowly defined at the time to exclude the flowering tops and resin derived therefrom, but still federally lawful if cultivated outside the United States) and would have effectively prohibited the theretofore lawful importation and sale of such non-psychoactive hemp foodstuffs with even trace amounts of THC.² In its ruling in *Hemp Industries Assoc. v. DEA*, the Ninth Circuit permanently enjoined the DEA from enforcing the CSA against manufacturers and importers of such products. The court held that the DEA could:

regulate foodstuffs containing natural THC if it is contained within marijuana, *and*
can regulate synthetic THC of any kind. *But they cannot regulate naturally-*

¹ This holding is still the current law, as the DEA did not appeal the Ninth Circuit's decision to the U.S. Supreme Court.

² See *Clarification of Listing of "Tetrahydrocannabinols" in Schedule I*, DEA 205-F (published March 21, 2003), [68 Fed. Reg. 14114-01](#), and *Exemption From Control of Certain Industrial Products and Materials Derived From the Cannabis Plant*, DEA 206-F (published March 21, 2003), [68 Fed. Reg. 14119-01](#).



Request for Hearing in Docket No. DEA-1362 and
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June 4, 2024

*occurring THC not contained within or derived from marijuana—i.e., non-psychoactive hemp products—because non-psychoactive hemp is not included in Schedule I. The DEA has no authority to regulate drugs that are not scheduled, and it has not followed procedures required to schedule a substance.*³

While it is absolutely true that THCA has the potential to convert to THC, this was already contemplated by Congress in its approach to defining “hemp”. Just as the DEA and federal courts acknowledge that Congress did not intend the threshold defined for Delta-9 THC to apply to Delta-8 THC, Congress could not have intended for the threshold defined for Delta-9 THC to apply to THCA.⁴ Congress was abundantly clear when it defined federally lawful hemp to include

“all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.”

Additionally, the [USDA already counts the THCA content in pre-harvested hemp toward the total THC concentration](#), so it serves no purpose for the DEA to attempt to classify THCA as “equivalent to THC” in contravention of Congress’ intent in both the CSA and 2018 Farm Bill.

Finally, as a matter of law THCA is currently *not* a scheduled controlled substance unless it’s specifically marijuana-derived. THCA ($C_{22}H_{30}O_4$) has a different chemical structure and molecular formula from THC ($C_{21}H_{30}O_2$), is *not* a “derivative” or “isomer” of THC (nor is it an analogue) and being non-intoxicating it does *not* display the same pharmacological activity as THC. Thus, as a different cannabinoid from THC, THCA would need to be scheduled before it could be legally deemed the functional equivalent of a Schedule I controlled substance. However, [THCA has never been through formal scheduling by the DEA](#), as an examination of the Federal Register proves.

Even as an immediate precursor of THC (per 21 USC §802(23)), THCA still can’t be deemed a Schedule I-equivalent based on the DEA’s response to individual correspondence (creating an “underground regulation”)—at a minimum, the DEA would need to first issue a formal order and publish it to the Federal Register (per 21 USC §811(e) and 21 CFR §1308.47).

Thank you for considering my comment on the subjects covered therein.

³ *Hemp Indus. Ass’n v. DEA*, 357 F.3d 1012, 1018 (9th Cir. 2004) (emphasis added).

⁴ See *AK Futures LLC v. Boyd St. Distro, LLC*, 35 F.4th 682 (9th Cir. 2022); see also Letter from Terrence L. Boos, Chief, Drug & Chem. Evaluation Section, Diversion Control Div., U.S. Dep’t of Just. Drug Enf’t Admin., to Donna C. Yeatman, Exec. Sec’y, Ala. Bd. of Pharmacy (Sept. 15, 2021), <https://hempindustrydaily.com/wp-content/uploads/2021/11/DEA-letter-to-AL-BOP.pdf>.



Request for Hearing in Docket No. DEA-1362 and
comment to same
June 4, 2024

Respectfully yours,

A handwritten signature in blue ink, appearing to read "Khurshid Khoja". The signature is fluid and cursive.

Khurshid Khoja

21 CFR 1316.47 (up to date as of 6/11/2024)
Request for hearing; answer.

21 CFR 1316.47 (June 11, 2024)

21 CFR 1316.47 (up to date as of 6/11/2024)
Request for hearing; answer.

21 CFR 1316.47(b)

- 1) state with particularity the interest of the person in the proceeding;
- (2) state with particularity the objections or issues concerning which the person desires to be heard; and
- (3) state briefly the position of the person regarding the objections or issues.

1) I have personally experienced the harms of the drug war on Cannabis within the VA Healthcare system causing a missed diagnosis, neglect, abuse, poisoning, and attempted murder to cover it up by our government. In addition to their plans of entrapment for me, and extensive hacking as well as interference with my small business I have been developing based on Vedic, Ayurvedic, and Yogic roots and other Ancient alternative healing modalities such as sound therapy and education on incorporating Cannabis use into these modalities for the entourage effects to be applied and directed effectively from my healing protocols as a Disabled Veteran dealing with PTSD and Neurotoxins among other Toxic elements from Jet Fuel exposure and a poisonous spider bite under my jaw from USMC barracks (I was one to pass the white glove test) and multiple serious adverse reactions to VA Pharmaceuticals and Vitamins, Treatments, Misdiagnosis's such as (Dissociative Identity Disorder), including multiple additional attempts on my life including with mold toxin exposure. I can no longer even eat conventional foods or at restaurants. There has also been substantial tampering of my food beverages as well as supplements with chemicals related to my detoxification process to include people involved in DEA operations placing themselves outside my door of my business and chain smoking to fill my business with the toxins as their front Food For Lane County creates a neighborhood drug den for DEA research and training this is bad for Local Businesses as well it is creating a false narrative when it comes to the use of substances including Cannabis.

2) Schedule Three is not good enough, we need full legalization. Our Government needs to face the facts. Schedule III will only create more problems and that is a Vastly understood and completely predictable situation.

3) my position for is for Full Legalization. I also have complete plans for a system that benefits everyone specifically our government financially.

21 CFR 1316.47 (up to date as of 6/11/2024)
Request for hearing; answer.

21 CFR 1316.47 (June 11, 2024)

21 CFR 1316.47 (up to date as of 6/11/2024)
Request for hearing; answer.

21 CFR 1316.47 (June 11, 2024)

This content is from the eCFR and is authoritative but unofficial.

Title 21 — Food and Drugs

Chapter II — Drug Enforcement Administration, Department of Justice

Part 1316 — Administrative Functions, Practices, and Procedures

Subpart D — Administrative Hearings

Authority: 21 U.S.C. 811, 812, 871(b), 875, 958(d), 965.

Source: 36 FR 7820, Apr. 24, 1971, unless otherwise noted. Redesignated at 38 FR 26609, Sept. 24, 1973.

§ 1316.47 Request for hearing; answer.

- (a) Any person entitled to a hearing and desiring a hearing shall, within the period permitted for filing, file a request for a hearing that complies with the following format (see the Table of DEA Mailing Addresses in § 1321.01 of this chapter for the current mailing address):

(Date) 06/12/2024

Drug Enforcement Administration, Attn: Hearing Clerk/OALJ Attn: Administrator. Attn: DEA Federal
Register Representative/DPW
(Mailing Address) 8701 Morrisette Drive, Springfield, Virginia 22152

Subject: Request for Hearing

Dear Sir:

The undersigned Sage Endoom Cannablisshum Docket No. DEA-1362
(Name of the Person) hereby requests a hearing in the matter of: (Identification of the proceeding).

(State with particularity the interest of the person in the proceeding.) See Next Page

All notices to be sent pursuant to the proceeding should be addressed to:

(Name) Sage Endoom Cannablisshum

(Street Address) 1304 Wilkshire Circle SW

(City and State) North Canton Ohio 44720

Respectfully yours,

(Signature of Person) 

- (b) A party shall file an answer as required under §§ 1301.37(d) or 1309.46(d) of this chapter, as applicable. The presiding officer, upon request and a showing of good cause, may grant a reasonable extension of the time allowed for filing the answer.

[87 FR 68045, Nov. 14, 2022]

21 CFR 1316.47(b) (enhanced display)

page 2 of 3

21 CFR 1316.47 (up to date as of 6/11/2024)
Request for hearing; answer.

21 CFR 1316.47(b)

- 1) state with particularity the interest of the person in the proceeding;
- (2) state with particularity the objections or issues concerning which the person desires to be heard; and
- (3) state briefly the position of the person regarding the objections or issues.

1) I have personally experienced the harms of the drug war on Cannabis within the VA Healthcare system causing a missed diagnosis, neglect, abuse, poisoning, and attempted murder to cover it up by our government. In addition to their plans of entrapment for me, and extensive hacking as well as interference with my small business I have been developing based on Vedic, Ayurvedic, and Yogic roots and other Ancient alternative healing modalities such as sound therapy and education on incorporating Cannabis use into these modalities for the entourage effects to be applied and directed effectively from my healing protocols as a Disabled Veteran dealing with PTSD and Neurotoxins among other Toxic elements from Jet Fuel exposure and a poisonous spider bite under my jaw from USMC barracks (I was one to pass the white glove test) and multiple serious adverse reactions to VA Pharmaceuticals and Vitamins, Treatments, Misdiagnosis's such as (Dissociative Identity Disorder), including multiple additional attempts on my life including with mold toxin exposure. I can no longer even eat conventional foods or at restaurants. There has also been substantial tampering of my food beverages as well as supplements with chemicals related to my detoxification process to include people involved in DEA operations placing themselves outside my door of my business and chain smoking to fill my business with the toxins as their front Food For Lane County creates a neighborhood drug den for DEA research and training this is bad for Local Businesses as well it is creating a false narrative when it comes to the use of substances including Cannabis.

2) Schedule Three is not good enough, we need full legalization. Our Government needs to face the facts. Schedule III will only create more problems and that is a Vastly understood and completely predictable situation.

3) my position for is for Full Legalization. I also have complete plans for a system that benefits everyone specifically our government financially.

**Aubree Adams**

+719-250-5740 📞

aubree@everybrainmatters.org 📧

www.everybrainmatters.org 🌐

6.13.2024

Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW
8701 Morrisette Drive
Springfield, Virginia 22152

Subject: Request for Hearing

Dear Sir:

The undersigned, Aubree Adams, hereby requests a hearing in the matter of: Docket No. DEA-136. Transferring marijuana from Schedule I of the Controlled Substances Act ("CSA") to Schedule III of the CSA.

My name is Aubree Adams, and I have a particular interest in rescheduling marijuana because of the harm it has caused my family and my community in Pueblo, Colorado. I am the founder and director of Every Brain Matters, a non-profit community formed by families who have experienced the detrimental effects of industrialized marijuana.

At Every Brain Matters, we challenge the misleading narrative that marijuana is a harmless exercise of personal freedom. Through scientific evidence and compelling personal stories, we highlight the reality that marijuana is a potent and addictive substance with the potential to cause significant harm. Like other addictive drugs, marijuana can and is devastating lives.

I object to lowering the schedule on marijuana because our communities are ill-equipped to prevent, manage, or aid recovery for individuals suffering from cannabis use disorder, cannabis-induced psychosis, or cannabinoid hyperemesis syndrome. The marijuana industry, driven by profit and predatory practices, spreads misinformation, targets vulnerable populations, and promotes addictive products disguised as sugary treats or medicine.

It is imperative that the voices of American families harmed by marijuana, including my own, are heard in the critical discussions around the rescheduling of this drug. Offering tax benefits and regulatory approvals for cannabis while families endure the loss of their financial stability and watch the health of loved ones deteriorate due to marijuana's effects is a profound social injustice.

Policy reforms must recognize that marijuana contributes significantly to the rise in addiction, mental health issues, homelessness, and violence. My goal is to advocate for policies that expose these truths and protect our communities from the predatory marijuana industry.

All notices to be sent pursuant to the proceeding should be addressed to:

Aubree Adams
1909 N. Elizabeth Street
Pueblo, CO 81003

Respectfully yours,
Aubree Adams

Director, Parent, Advocate

6.15.2024

Drug Enforcement Administration, Attn: Administrator
8701 Morrisette Drive
Springfield, Virginia 22152

Subject: Request for Hearing

Dear Sir:

The undersigned, Heidi Anderson-Swan, hereby requests a hearing in the matter of Docket No. DEA-136. Transferring marijuana from Schedule I of the Controlled Substances Act ("CSA") to Schedule III of the CSA.

I am currently working with Bryn Spejcher. Ms. Spejcher was recently convicted of involuntary manslaughter while she was in an acute state of cannabis-induced psychosis. Although she was convicted by a jury of her peers, the judge said there was no way Ms. Spejcher could have known that using cannabis could make her psychotic or become violent. Part of Ms. Spejcher's sentencing is to educate the public about cannabis-induced psychosis.

I attended every day of the trial. I had particular interest in this trial, in part, because I work with a nonprofit that educates about the harms of marijuana, Every Brain Matters (EBM). Since the trial ended, EBM has been approved by Ms. Spejcher's probation officers to be the one and only nonprofit to help Ms. Spejcher fulfill her community service hours to educate about what marijuana can do to some people. This is a dire need in our country today. Most Americans have never heard marijuana can cause a person to lose touch with reality, have visual and audible hallucinations and then act out violently based on them. I am a speaker and have done presentations on these topics. I am told frequently that I am the first person to tell them about the harms. This is inexcusable. If people can be convicted of their actions while in cannabis-induced psychosis, they should have informed consent about all of the risks before they choose to use it. As it is, the marijuana industry is withholding the growing science about the mental health harms of their products which gives the impression their products are benign.

If marijuana is rescheduled, then the perception of safety will only increase. Although what happened with Ms. Spejcher is uncommon, EBM has independently researched and found over a dozen cases from around the world where the perpetrator was convicted of violence while in cannabis-induced psychosis. See document.

More: The killing occurred on May 28, 2018 in Thousand Oaks, California. This was only months after legalization was implemented. There were no warnings about the mental health harms of marijuana, nor are there any today. It's a subject I am well-versed in because I have been trying to educate the public about it since 2017 when I published the first fictional story to illustrate cannabis-induced psychosis. It's called *A Night In Jail*. Using the book as a platform, I have reached out to public health organizations, educational systems, mental health organization and the media. The overwhelming response I have received has been that they ignore the studies showing the risks. They also refuse to pass the information along to the public.

Additionally, I volunteered with two bills in the California Legislature to put basic protections on high THC products. One to provide mental health warnings, not dissimilar to what we have on cigarettes, and the other was to provide protections so that toddlers would not mistake highly psychoactive candies as something they would eat. Both of these commonsense bills failed due to pressure from the industry. So we have no consumer protections in California.

This sets the stage for what happened to Ms. Spejcher and the friend she tragically killed, Chad O'Melia. They are both victims of the misinformation provided by this addiction industry, the California Legislature, the media and public health organizations. Originally from Illinois, Ms. Spejcher is a Doctor of Audiology. She was newly employed with UCLA to set up their satellite office in Thousand Oaks. She has never used drugs illegally. She has only used marijuana less than ten times in her life. She met Chad O'Melia at a dog park. He was a daily user. This did not raise a red flag to her because she had heard: *it's legal, it's safer than alcohol, you can't overdose on it*. Mr. O'Melia gave Ms. Spejcher a massive amount of THC all at one time. Being a naïve user, she believed the industry's messaging and assumed all marijuana was mild with no negative consequences. After ingestion, she lost touch with reality and lost control of her body. In and out of consciousness, she watched her own actions as she stabbed Mr. O'Melia to death. She then stabbed herself in her own neck. When the officers broke in, they had to tase her and beat her with a baton to get her to stop stabbing herself. Had they not intervened, she would not have survived.

The public is uninformed. Marijuana should stay in Schedule I.

All notices to be sent pursuant to the proceeding should be addressed to:

Heidi Anderson-Swan
736 Gould Ave #6
Hermosa Beach, California 90254

Respectfully yours,


Heidi Anderson-Swan

Speaker, writer, advocate, producer



EVERY
BRAIN
MATTERS



THC-Psychosis and Violence

The following is a list of violent incidents in which cannabis use or cannabis-induced psychosis played a role in the criminal charges and sentences. The attacks took place in several different countries, and the attackers were of varied races and ethnicities. Several perpetrators regained lucidity after stopping cannabis use. The sentences vary wildly from no jail time to 50 years in prison, but none were convicted of first-degree murder.

The incidents have several similarities:

- Most had a sudden onset of violent behavior.
- Knives or other sharp objects were used as the weapon.
- The perpetrator had no motive.
- Violence incidents were against family or friends with whom the perpetrator had no animosity.
- Violent acts were brutal.
- The perpetrator did not plan or try to conceal the crime.
- The perpetrator did not seem to feel pain when police used physical force to stop the assault.
- The age of the perpetrators was mainly in their twenties or early thirties, with some older.
- Gender was overwhelmingly male.

2024—Rockford, Illinois—Christian Soto, 22, is facing four counts of first-degree murder after he stabbed and killed four people after using marijuana supplied by his friend whom he killed. He claims the marijuana was laced, and he became psychotic and grabbed a knife from the kitchen. (Ongoing).

2024 – Dublin - Diego Costa Silva was found not guilty by reason of insanity due to cannabis-induced psychosis when he killed and decapitated his wife. Both psychiatrists agreed that the psychosis was not due to acute intoxication of the drug but a more persistent illness of cannabis-induced psychosis, with the court hearing that the accused persisted in displaying psychotic symptoms eleven days after he was arrested and detained. Silva believed his wife was a serpent, and he had to cut off her head after strangling and stabbing her to make sure she was dead.

2024 - California – Bryn Speicher killed O'Melia in Thousand Oaks, California, when she was 28. The charge was reduced from 2nd-degree murder when the prosecution expert

determined she had an episode of cannabis-induced psychosis after being given cannabis in a bong by O'Melia. She stabbed O'Melia 108 times and then stabbed herself. Police tased her and used their baton nine times before she dropped the knife.

2023 -Pennsylvania – Babysitter Lavrius Watson, 28, was sentenced to 15-40 years after pleading guilty to 3rd-degree murder. He stabbed and killed a 41-year-old mom of kids he was babysitting with a kitchen knife after they shared marijuana cookies, and he had an adverse reaction.

2021- Iowa - Paul Belk, 32, was sentenced to 50 years in prison for stabbing his mother 16 times with a knife and scissors in 2020. He must serve 35 years before being eligible for parole. The defense said he was insane at the time; the judge said his marijuana use kept him from forming intent, so the judge convicted him of 2nd degree instead of first-degree murder.

2021 - UK Jacob Notman, 28, pled guilty to manslaughter for stabbing his girlfriend 30 times after eating a marijuana brownie. He was cleared of murder due to lack of intent after the crown heard evidence that he was having a psychotic break due to the "bad cannabis trip." The phone video recorded the horrific attack. The judge said cannabis can be very dangerous. "It is an illegal drug for good reason."

2021—France—Kobili Traore, France's highest court, ruled that Traore would not have to stand trial for the 2017 killing of a Jewish woman by throwing her over a balcony. Traore was a heavy cannabis smoker who was found to have been "delirious" at the time and, therefore, not responsible. He had been in psychiatric care since the event. The ruling drew widespread protests.

2021—Seattle—Buckey Wolfe, 26, was charged with 2nd-degree murder for killing his brother with a 4-foot-long sword in 2018; Wolfe was under the delusion that his brother was a lizard. His social media posts, which were taken down, show psychotic posts and cannabis use. Some family members said Buckey should "smoke more pot to calm himself down."

2020- Edmonton, Canada – Jason Dickout pled guilty to manslaughter after being charged with 2nd-degree murder and was sentenced to 3 years and nine months for stabbing and killing his mother in 2017 when he was 30. He had used marijuana with his sister, and the court determined he had an episode of extreme but "transient cannabis-induced psychosis." And the court concluded that without cannabis, the incident would not have occurred. He was also sentenced to treatment and three years probation.

2020—Japan - Satoshi Uematsu, 29, was found guilty of 2016 stabbing and killing 19 people and injuring 26 in a care facility where he had worked and sentenced to death. His defense had been planning to argue that he had had cannabis-induced psychosis at the time (which had been previously diagnosed.) He was found competent to stand trial. As of 2022, he was appealing his sentence.

2019 – British Columbia – Adam Kehl, 30, pled guilty to manslaughter and was sentenced to 5 years less time served for stabbing and beheading his father in 2018. He was judged to have been suffering from "cannabis-induced psychosis." A heavy cannabis user became psychotic after using during a gathering of 14 people. He was heard howling like a wolf and was seen stabbing at his father's body. He seemed oblivious when police shot him with rubber bullets. He had no psychotic episodes since the attack. "Adam said he was unaware cannabis could lead to such a thing and, had he known, he would never have started."

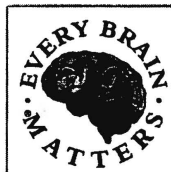
2018—Ontario, Canada—Mark Phillips, 36, a lawyer, pled guilty to one count of assault reduced from aggravated assault when he attacked an immigrant family with a baseball bat in 2017. He was given no jail time. He claimed to be suffering from cannabis-induced psychosis. He had smoked several joints on the day of the attack. After stopping the use of cannabis in jail, he became clear-headed.

2017—Colorado—Richard Kirk, 50, pled guilty to 2nd-degree murder for killing his wife in 2014 with a gun after eating a marijuana edible and was sentenced to 30 years. Kirk had initially pled not guilty because of insanity but changed his plea to avoid a trial for 1st-degree murder and life in prison. The defense had been planning to say he was suffering from psychosis after eating the marijuana; only THC was found in his system.

2015 – Melbourne, Australia – Easton Woodhead, 20, was found not guilty of murder for the stabbing death of a homeless man due to "mental impairment." He had been smoking cannabis daily and believed he was the son of a werewolf. The defense asserted he was suffering acute psychosis and pointed out he turned the knife on himself at some point.

2007 - Thousand Oaks, California – Calvin Sharp was sentenced to life without parole for stabbing a 6-year-old boy to death with a meat cleaver and injuring two others. The defense argued he was a paranoid schizophrenic, but the prosecution said he was in a marijuana-induced and "fluctuating" psychosis. The judge did not accept that Sharp was insane at the time of the crime.

1983—British Columbia—Bruce Blackman, 22, was found incompetent to stand trial after being accused of first-degree murder for the killing of 6 family members. Blackman was a heavy user of cannabis and used cannabis prior to the murders. He had been experiencing psychotic symptoms for some weeks and paranoid delusions.



EveryBrainMatters.org

June 16, 2024

Drug Enforcement Administration,

Attn: Administrator- DEA Federal Register Representative/DPW- Hearing Clerk/OALJ

8701 Morrisette Drive, Springfield, Virginia 22152.

Subject: Request for Hearing

Dear Sir:

The undersigned David Heldreth hereby requests a hearing in the matter of: DEA rule proposal: Schedules of Controlled Substances: Rescheduling of Marijuana also identified as Docket No. DEA-1362 and A.G. Order No. 5931-2024.

(1) state with particularity the interest of the person in the proceeding; (2) state with particularity the objections or issues concerning which the person desires to be heard; and (3) state briefly the position of the person with regard to the objections or issues.

I would like to verify standing in the rule-making by asserting that:

- 1.) David Heldreth is currently not licensed by the DEA.
- 2.) David Heldreth uses cannabis for nerve pain and related issues. Moving marijuana and related items to schedule 3 will not increase my access to the use of THC/marijuana and related items for medical use. Rather the government/HHS/FDA/DEA should have, based on the evidence found it should be de-scheduled.
- 3.) David Heldreth has research, IP and patent filings that incorporate marijuana, cannabis, THC and related items.
- 4.) David Heldreth will be harmed if marijuana is moved into Schedule 3 instead of being de-scheduled and will be disadvantaged compared to those people and entities that have schedule 3 licensing. Rather than schedule 3, marijuana should be de-scheduled.

Now in regards to the current rule-making, let us begin:

- A) To start there are apparent errors in the rulemaking process, in that the DEA did not consult with tribal governments as required under Executive Order 13175.

The rulemaking references active Executive Order 13175 - Consultation and Coordination with Indian Tribal Governments – however, it asserts that no such consultation with tribal governments is necessary, or as stated directly below:

"This proposed rule does not have tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes."

This statement is incorrect as this rulemaking will change the status of a substance under federal law from Schedule 1 to Schedule 3 it will then as such require changes to tribal law enforcement, tribal health care via independent or Indian Health Services, and other programs. Reservations are

regulated as federal lands and many tribal law codes reference federal law and the Controlled Substances Act. As such the current rulemaking will create a situation in which tribal governments and law enforcement will be required to train law enforcement on the new laws and this alone will impose direct costs on tribal entities and governments. Additionally, the costs of any enforcement of these new laws incurred from arrests, testing, jailing, etc. which falls on tribal governments again represent burdens and reasons for the DEA/Department of Justice to conduct a tribal consultation prior to rulemaking as is required under EO 13175. From the text:

"To the extent practicable and permitted by law, no agency shall promulgate any regulation that has tribal implications, that imposes substantial direct compliance costs on Indian tribal governments, and that is not required by statute, unless:

- (1) funds necessary to pay the direct costs incurred by the Indian tribal government or the tribe in complying with the regulation are provided by the Federal Government; or*
- (2) the agency, prior to the formal promulgation of the regulation,*
 - (A) consulted with tribal officials early in the process of developing the proposed regulation;*
 - (B) in a separately identified portion of the preamble to the regulation as it is to be issued in the **Federal Register**, provides to the Director of OMB a tribal summary impact statement, which consists of a description of the extent of the agency's prior consultation with tribal officials, a summary of the nature of their concerns and the agency's position supporting the need to issue the regulation, and a statement of the extent to which the concerns of tribal officials have been met; and*
 - (C) makes available to the Director of OMB any written communications submitted to the agency by tribal officials."*

Additionally, under the current DOJ tribal consultation policy, the DEA and DOJ are tasked to not narrowly define when it is necessary to consult tribal governments, but to do so in a way that is widely encompassing and to err on the side of consulting, rather than not. From the DOJ's own tribal consultation policy:

"The requirements of Executive Order 13175 and this Policy Statement generally will be construed liberally in favor of Consultation on any given policy as defined above with Tribal implications. Consultations may be organized in a variety of ways, from a single group discussion to a more iterative process involving a series of discussions. All decisions regarding whether and how to conduct a Consultation, or whether a given policy or topic has Tribal implications, will be coordinated with the Department's Office of Tribal Justice."

There are 574 federally recognized tribes and around 258 tribal law enforcement agencies. That is a large amount of affected tribal entities and a large impact. As such I ask that the DEA withdraw the current rulemaking and begin the mandated tribal consultation process under EO 13175 and DOJ's own policy. The DOJ policy also requires notice at least 30 days before the date of consultation.

As such David Heldreth requests the rulemaking at hand be:

1. Withdrawn; and conduct tribal consultation which begins with a publication of notice seeking tribal input before rulemaking. The rule can be re-submitted for public comment and hearings after this is done.
- B) The next issue at hand that must be dealt with is, the DEA's current rulemaking references the Regulatory Flexibility Act

David Heldreth is a shareholder in Panacea Plant Sciences, itself is a small business that qualifies under the Regulatory Flexibility Act to have consultation. PPS researches cannabis, does not have a DEA license, and has had to keep focus on hemp due to federal law, except when working with groups in other countries. Moving marijuana into schedule 3 from schedule 1, instead of de-scheduling will hurt PPS and give preferential treatment to those with DEA schedule 3 or other licenses.

There are hundreds to thousands of hemp farms that would qualify under similar circumstances. There are also universities and other entities which would qualify. As such there is ample reason to follow the Regulatory Flexibility Act.

From the Regulatory Flexibility Act:

"§ 602. Regulatory agenda

- (a) During the months of October and April of each year, each agency shall publish in the Federal Register a regulatory flexibility agenda which shall contain —*
- (1) a brief description of the subject area of any rule which the agency expects to propose or promulgate which is likely to have a significant economic impact on a substantial number of small entities;*
 - (2) a summary of the nature of any such rule under consideration for each subject area listed in the agenda pursuant to paragraph (1), the objectives and legal basis for the issuance of the rule, and an approximate schedule for completing action on any rule for which the agency has issued a general notice of proposed rulemaking, and*
 - (3) the name and telephone number of an agency official knowledgeable concerning the items listed in paragraph (1).*
- (b) Each regulatory flexibility agenda shall be transmitted to the Chief Counsel for Advocacy of the Small Business Administration for comment, if any.*
- (c) Each agency shall endeavor to provide notice of each regulatory flexibility agenda to small entities or their representatives through direct notification or publication of the agenda in publications likely to be obtained by such small entities and shall invite comments upon each subject area on the agenda.*
- (d) Nothing in this section precludes an agency from considering or acting on any matter not included in a regulatory flexibility agenda, or requires an agency to consider or act on any matter listed in such agenda."*

We would like to let it be known that this rulemaking was not included on the DOJ or DEA Regulatory Flexibility Agenda. We would like the rulemaking withdrawn until this can be done.

As such David Heldreth requests the rulemaking at hand be:

Withdrawn; and hold a small business and entity consultation which begins with a publication to that end prior to rulemaking in 2024 and potential final rulemaking in 2025.

C) David Heldreth disagrees with the proposed placement of marijuana in Schedule 3, and instead finds that it should rather be removed from control completely and de-scheduled.

Although, international treaties may tie the United States to controlling marijuana, THC and other compounds; it is unlikely that this treaty violation will lead to any negative outcome. Canada has similarly moved to make marijuana a medicine and even went further to make it a regulated recreational item. There has been no backlash to this move and no consequences for them. As such the UN and the treaty parties are in effect silently complicit.

If marijuana is placed into a schedule, it should rather than schedule 3, be placed into schedule 5 due to its relative safety.

Additionally, cocaine was allowed as an unapproved by the FDA drug for medical use until 1919, when it was approved under branded formulations by several companies.

<https://www.fda.gov/drugs/unapproved-drugs/fda-notification-regarding-cocaine-hydrochloride-solution-products>

However, the allowance as an unapproved drug use, was via grandfathering, but that was on the principal that the cocaine was pure and always an exact item in the grandfathered drug formulations from prior to 1938. Cocaine is and was derived from a plant source, Erythroxylaceae coca, which produces several tropane alkaloids and other compounds. In fact, most cocaine is not pure cocaine, but rather a mixture of compounds extracted from the plant, unless chemically purified in a modern lab. This is important because there have been attempts to have marijuana allowed as a drug for medical use via the same grandfathering mechanism that allowed cocaine as an FDA-unapproved drug to be used for medical use. However, the DEA/HHS/FDA denied that petition saying that they cannot verify the contents of the pre-1938 drug compounds as they are only labeled as marijuana flower or extract and not by compound (ie THC, CBD) However, again cocaine was allowed with unknown variation, but due to this same type of variation, this medical marijuana grandfather petition was denied.

<https://www.regulations.gov/document/FDA-2011-P-0671-0001>

This and the move to block wider access to cocaine for medical use, but instead only allow pharmaceutical branded approved versions, appear to be a move to consolidate the wider industry and supply of medicines into a small group of companies and people.

I make these points to argue that raw dried marijuana flower and marijuana/marijuana extract and/or tinctures should be allowed to be manufactured by DEA-licensed marijuana cultivators, manufacturers and compound pharmacies. Marijuana should then be allowed to be prescribed by doctors nationwide and filled by pharmacies.

Grandfathering (exempting from DEA/FDA regulation) state medical cannabis producers would also be a potential option.

Additionally, patients should be allowed to seek a prescription and if granted to seek a DEA license as a manufacturer and distributor/dispensary to cultivate/dispense their own medical cannabis, or to do so in a collective with other patients. Patients could also import from Canada if allowed. The DEA is currently entering into agreements with religious organizations and churches to allow for their cultivation/importation and use of schedule 1 substances. If these smaller, non-commercial organizations are being allowed to have DEA licenses, then there is no reason why such a similar scheme could not be developed to provide access to the medical patients in the United States that wish to have immediate access, and to control their own supply of medication.

<https://www.marijuanamoment.net/federal-settlement-will-allow-arizona-church-to-import-process-and-use-ayahuasca-as-religious-sacrament/>

If the DEA, FDA, HHS and related agencies do not either, approve raw cannabis/extracts/tinctures as a FDA approved medication, provide a grandfather option via FDA/DEA as unapproved, but allowed medications, or allow state medical cannabis to be federally legal, then this rule-making does nothing to provide access to patients, and is effectively worthless except that providing 280E tax relief for federally illegal state medical cannabis businesses. There will be no reduction in costs or difficulty for research by this rule-making either, the only effective difference for research in schedule 1-3 is which box is checked on forms.

However, although marijuana as a botanical product and medicine may be safe, there are risks from marijuana and cannabis derivatives and products which has been seen in the public via the EVALI, lung injury vaping outbreak in 2020, 2,800 people were harmed and 68 died.

<https://www.yalemedicine.org/conditions/evali>

This outbreak primarily affected cannabis and hemp markets. One of the problems is the lack of regulations and the often lax regulations at the state levels. This leads to unregulated flavors/terpenes/cutting agents, from non-cannabis sources being added. For example vitamin e acetate, creating issues in the lungs with EVALI was cited primarily via the acetate. However, companies in the hemp industry are now creating products with THC-O-Acetate that are inhaled, creating similar dangers.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9813278/>

Squalane was another large problem in Oregon, and other states. Squalane was sold by companies as a diluent.

<https://mjbizdaily.com/oregon-cannabis-regulators-ban-additives-first-seen-in-vaping-crisis/>

Mold and pesticides are also common in the state marijuana industry, and often under or un-reported. Testing is not done at the appropriate frequency and intensity for product safety. For example, Washington State only does pesticide testing of marijuana on random testing that takes years for every company to be tested. As such it took years for the state's marijuana regulator to find out that DDT derivative DDE had been identified in marijuana products, likely due to the farmland being used for other crops previously. A bulletin from the regulator on the issue can be found here: <https://content.govdelivery.com/accounts/WALCB/bulletins/36473ba>.

As such, David Heldreth asks the government to regulate cannabis, hemp and marijuana products for safety, and use this rule-making to also apply the deeming rule under tobacco inhalation product rules to require the products to be held to the same standards of safety at a minimum if unscheduled.

However, if placed into Schedule 3, 4 or 5, due to the myriad problems with essentially, every state medical or recreational marijuana and hemp programs, David Heldreth asks the government to regulate medical marijuana standards at a federal level so that the country has a consistent, fair, safe market for patients and business.

D) The DEA ALJ we believe is unconstitutional as similar ALJ schemes have been found so by the Supreme Court. As such I believe that this rule-making should if hearings are held, be heard instead of the ALJ in federal court. Also there are Chevron deference issues. These all likely are being addressed, while indirectly, in the Supreme Court via the Jarkesy v SEC lawsuit. As such I hold that the currently rule-making should be stayed until the Jarkesy ruling is final.

Further evidence and information will be presented in the future.

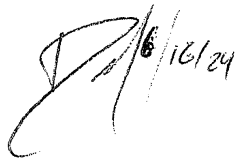
All notices to be sent pursuant to the proceeding should be addressed to:

David Heldreth

14321 Se 49th St

Bellevue WA 98006

Respectfully yours,



Drug Enforcement Administration
Attn: The Honorable Anne Milgram, Administrator
8701 Morrisette Drive
Springfield, Virginia 22152

Drug Enforcement Administration
Attn: Hearing Clerk/OALJ
8701 Morrisette Drive
Springfield, Virginia 22152

Drug Enforcement Administration
Attn: DEA Federal Register Representative/DPW
8701 Morrisette Drive
Springfield, Virginia 22152

June 16th, 2024

**Re: Request for Hearing
Docket No. DEA-1362**

Dear Administrator Milgram,

The undersigned, National Drug and Alcohol Screening Association (NDASA) hereby requests a hearing in the matter of: Docket No. DEA-1362; A.G. Order No. 5931-2024, "Schedules of Controlled Substances: rescheduling of Marijuana". In accordance with 21 U.S.C. 811 and 812, the purpose of this requested hearing would be to "receiv[e] factual evidence and expert opinion regarding" whether marijuana should be transferred to schedule III of the list of controlled substances.

The Notice of Proposed Rulemaking (NPRM) issued in this matter contains a significant number of factual inaccuracies. In accordance with 21 CFR sections 1308.44(a) and 1316.47(a), we respectfully request that you grant a hearing on the record to consider the factual documentary evidence and expert witness testimony we would proffer to prove factual inaccuracies submitted by the Department of Health and Human Services (HHS) and upon which the Drug Enforcement Administration (DEA) and the

Attorney General are expected to rely for the decision about rescheduling marijuana from Schedule I to Schedule III under the Controlled Substances Act (CSA).

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to “receiv[e] factual evidence and expert opinion regarding” whether marijuana should be transferred to schedule III of the list of controlled substances. We recognize the HHS’s scientific and medical determinations are accorded “significant deference” through the rest of the rulemaking process. However, scientific and medical determination based on flawed factual assumptions and incorrect data should not be afforded such deference. We respectfully submit that flaws in reasoning and incorrect factual assertions should be addressed by an administrative law judge, as the decider of fact, in this formal rulemaking process.

Before a final decision is reached on rescheduling, we respectfully request a hearing on the factually incorrect assertions of HHS, upon which the DEA and the Attorney General are relying in the proposal to make marijuana a Schedule III drug under the Controlled Substances Act. It is essential that the final rule rests upon solid reasoning and reliable facts.

Statements required per 21 CFR 1308.44(a) and 1316.47(a)

I. State with particularity the interest of the person in the proceeding.

NDASA’s interest in this matter is to continue protecting commercial and public transportation safety. Our non-profit association, NDASA, represents a diverse coalition of employers and contractors, including medical professionals, substance abuse professionals, laboratory and toxicological experts, certified drug and alcohol collections

professionals, designated employer representatives, major transportation industry employers and their professional associations, large and small business owners, who are on the front lines of protecting the traveling public via safe operations of commercial and public transportation in our nation. Our membership reaches tens of thousands of employers and millions of American workers nationally.

NDASA and its membership are extremely concerned about the unintended consequences of rescheduling marijuana from Schedule I to Schedule III of the CSA. Specifically, such rescheduling would end the United States Department of Transportation's (DOT) ability to test safety-sensitive transportation employees for marijuana drug testing and effect deterrence for commercial transportation safety-sensitive employees across the nation. Transportation safety sensitive employees include, but are not limited to: airline pilots, air traffic controllers, school bus drivers, subway and train operators, ferry operators, pipeline operators and truck drivers. These safety-sensitive employees have been subject to testing for marijuana and other drugs since shortly after catastrophic accidents caused by marijuana use occurred in the mid and late 1980s.

Rescheduling marijuana to Schedule III would abruptly end DOT-regulated testing for marijuana would have a profoundly detrimental impact on transportation safety in the United States, potentially endangering American citizens. As mentioned above, our members are on the front lines of protecting the safety of commercial and public transportation nationwide. We are deeply invested in maintaining effective measures to prevent needless accidents caused by those under the influence of marijuana and other impairing substances.

The connection between the rescheduling of marijuana and the impact on commercial transportation safety was never discussed in the NPRM in this docket, so it is fair to conclude that there is a significant and dangerous blindside in this rulemaking. On the Federal side, air traffic controllers employed by the Federal Aviation Administration (FAA) would also no longer be subject to the deterrence and detection ensured by Federal marijuana testing. It is in NDASA's interest to raise these issues to the attention of the DEA and the Attorney General – to prevent potentially catastrophic accidents and loss of life as a result of the rescheduling of marijuana.

This important connection to the rescheduling of marijuana and transportation safety that was not addressed in the NPRM was created through the Omnibus Transportation Employees Testing Act of 1991 (OTETA), codified at 49 U.S.C. 45102 and 45104 (aviation industry testing), 49 U.S.C. 20140 (rail), 49 U.S.C. 31306 (motor carrier), and 49 U.S.C. 5331 (transit). OTETA requires the DOT to follow the Substance Abuse and Mental Health Services Administration of HHS for the science of drug testing, including the drugs and cutoffs, which are set forth in the HHS Mandatory Guidelines. OTETA also requires DOT to use only HHS-certified laboratories for all drug testing required by DOT.

However, HHS does not have authority to test for Schedule III drugs. The authority of HHS to test for and to certify laboratories for testing is provided by Executive Order 12564– Drug-free Federal Workplace of Sept. 15, 1986 (E.O. 12564). Under E.O. 12564. HHS is only authorized to test for drugs and certify laboratories to test for drugs that are in Schedule I or II for the CSA. Specifically, E.O. 12564, Section 7(c) states: “For purposes of this Order, the term ‘illegal drugs’ means a controlled substance included in

Schedule I or II, as defined by section 802(6) of Title 21 of the United States Code”.¹

Sections 3.2 (a) of both the HHS Mandatory Guidelines for Urine and the HHS Mandatory Guidelines for Oral Fluid state that an employee may be tested for “any drugs listed in Schedule I or II of the Controlled Substances Act.”²

If marijuana becomes a Schedule III substance, HHS would no longer be able to test for or certify laboratories to test for marijuana. As a result, DOT immediately would no longer be able to test for marijuana because OTETA requires DOT to rely on HHS for the science of drug testing (the drug cutoffs and scientific protocols), as well as conducting all DOT-regulated testing through HHS certified laboratories.

Hence, the rescheduling of marijuana to Schedule III would stop all DOT-regulated testing for marijuana, which we believe is a profound unintended consequence. If marijuana becomes a Schedule III substance, safety-sensitive transportation employees, including airline pilots, air traffic controllers, school bus drivers, subway and train operators, ferry operators, pipeline operators and truck drivers, will no longer be subject to Federally regulated marijuana testing and would be able to use it. In addition, FAA’s air traffic controllers would be able to use marijuana and would not be subject to testing for it. The absence of marijuana testing for these safety-sensitive transportation employees poses a significant risk to the safety of our roads, skies, waterways, pipelines and rails.

¹Executive Order. *Federal Register*. [Online] [Cited: September 25, 2019.] <https://www.archives.gov/federal-register/codification/executive-order/12564.html> .

² HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs using Urine. 82 Fed. Reg. 7920 (Jan. 23, 2017) <https://www.govinfo.gov/content/pkg/FR-2017-01-23/pdf/2017-00979.pdf> ;HHS Mandatory Guidelines for Federal Workplace Drugtesting Programs using Oral Fluid. 84 Fed. Reg. 57554 (Oct. 25, 2019) <https://www.govinfo.gov/content/pkg/FR-2019-10-25/pdf/2019-22684.pdf>

Federally regulated drug testing for transportation safety-sensitive employees has long been integral to maintaining safety standards within the domestic transportation sector since several marijuana-related train and subway accidents took place in the 1980s. For more than three decades, these protocols have effectively prevented marijuana-related accidents in commercial transportation. In the more than 35 years of federally regulated drug testing, the National Transportation Safety Board has not found a single commercial transportation accident to have been caused by marijuana. Thus, the prevention resulting from DOT-regulated testing has created an outstanding record of safety that is at risk of being shattered by the rescheduling of marijuana.

NDASA believes the marijuana rescheduling proposal in the NPRM, which is based on many incomplete and erroneous factual evidence, would produce unintended and potentially catastrophic consequences. The proposal needs to be set aside or there would need to first be “Safety Carve-Out” to ensure that transportation safety-sensitive employees, including Federal air traffic controllers, would continue to be deterred from marijuana use. Such a Safety Carve-Out must ensure that HHS would continue to certify laboratories for substances below Schedules I and II of the CSA. A Safety Carve-Out could be accomplished through an Executive Order, legislation, or another definitive source to provide HHS with the authority to continue to set the testing procedures for marijuana and to certify laboratories to test for it – for the purposes of transportation safety. If this is not addressed through an Executive Order, then NDASA has an interest in seeing this debate moved to the U.S. Congress and, respectfully, not attempted to be resolved by the Executive Branch of the U.S. Government.

II. State with particularity the objections or issues concerning which the person desires to be heard.

NDASA will explain and provide evidence, including expert testimony at the hearing, as to why many of the HHS assertions set forth as foundational reasoning for rescheduling marijuana are incorrect. The impact of rescheduling marijuana based on faulty assumptions is potentially catastrophic to transportation safety in the United States.

We will present documentary evidence and expert testimony to correct the inaccuracies HHS has provided to the DEA under the eight factors set forth in 21 U.S.C. 811(c) the Attorney General must consider for rescheduling:

1. The drug's actual or relative potential for abuse.

“A. Whether there is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.” 99 FR 44597, 44601 (May 21, 2024)

In its analysis, HHS concluded “the vast majority of individuals who use marijuana are doing so in a manner that does not lead to dangerous outcomes to themselves or others.” *Id.* NDASA will offer information and studies to show the dangerous outcomes to individuals using marijuana are not so limited and, contradictory to the conclusions of HHS, “that the public-health risks posed by marijuana are lower compared to those posed by other drugs of abuse (e.g., heroin, oxycodone, cocaine), based on HHS’s evaluation of various epidemiological databases for emergency department (“ED”) visits, hospitalizations, unintentional exposures, and most importantly, overdose deaths.” *Id.*

NDASA would submit for consideration, as DEA anticipates, “additional data on seizures of marijuana by law enforcement, cannabis-related ED visits, as well as updated epidemiological survey data since 2022.” Id. at 44602

“B. Whether there is significant diversion of the drug or drugs containing such a substance from legitimate drug channels.” – Id. at 44602

NDASA will offer documentary evidence, as well as expert testimony, that contradicts the HHS finding “that there is a lack of evidence of significant diversion of marijuana from legitimate drug channels.” Id. at 44602 In fact, NDASA questions whether it is possible to create a presumption that there are currently “legitimate drug channels” for this Schedule I drug. In addition, in May of 2024, the DEA’s National Drug Threat Assessment 2024. We think DEA made valid points that we would like to address at a hearing on the following:

Given this unique landscape, DEA believes that the lack of data indicating diversion of marijuana from federally sanctioned drug channels to the illicit market is not indicative of a lack of potential for abuse of the drug. DEA anticipates that additional data on diversion from State programs and DEA-registered manufacturers may aid in a determination of whether diversion is taking place. Id. at 44602

“C. Whether individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of their professional practice.” – Id. at 44602

HHS admits that “[o]utside of the Federal- and State-sanctioned medical use of marijuana, individuals are using marijuana on their own initiative for medical, as well as nonmedical, purposes.” Id. at 44602. In addition, HHS cites 2022 data from the National

Survey on Drug Use and Health (NSDUH) that found 61.9 million people used marijuana in the last year. We will offer expert testimony to support that it is an erroneous conclusion to determine that it is acceptable within the criteria for Schedule III of the CSA to move marijuana in light of this data.

“D. Whether the drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that it will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that they have a substantial capability of creating hazards to the health of the user or to the safety of the community.” – Id. at 44602.

Marijuana is not a new drug and it has a potential for abuse proven by its current prevalent use and its supply chain through illegal sources, including drug cartels. The medical and recreational use of marijuana in the US at levels of potency from 5% tetrahydrocannabinol (THC) to 90% THC. NDASA will offer expert testimony to show HHS has understated its conclusion that marijuana “has the potential for creating hazards to the health of the user and to the safety of the community” Id. at 44603. In addition, we will provide expert testimony to contradict the HHS statement that “marijuana is not typically among the substances producing the most frequent incidence of adverse outcomes or severity of substance use disorder.” Id. at 44603

In response to the 2016 petition for rescheduling marijuana to Schedule III (81 FR 53688, Aug. 12, 2016) DEA and HHS both found that marijuana had a high potential for abuse. In response to DEA’s request in the NPRM, NDASA would like the opportunity to provide sources of additional data to assess marijuana’s actual or relative potential for abuse.

2. Scientific evidence of its pharmacological effect, if known;

There is an extensive discussion on pages 44603- 44606 about studies HHS conducted through SAMHSA and FDA. In the information provided, SAMHSA admits marijuana is addictive. We will provide evidence to underscore data on addiction that would merit keeping marijuana as Schedule I substance. We will also provide evidence to address the following concern: “DEA believes that additional data on marijuana’s pharmacological effects may be appropriate for consideration in assessing this factor.” – Id. at 44606

3. The state of current scientific knowledge regarding the drug or other substance;

We will offer expert testimony and documentary evidence lacking in the docket to address the state of current scientific knowledge about marijuana. Incidentally, we would provide expert testimony to substantiate that there are a broad range of products within the CSA’s definition of marijuana.

Also, it is important to note that HHS made the following statement, with which we agree and would discuss further at the hearing. This statement is actually contradictory to making a finding in support of rescheduling:

Products sourced from State-authorized adult-use and medical-use programs are subject to a patchwork of inconsistent product standards and safety requirements. Although some State programs have a set of standards (for example, on manufacturing, testing, labeling, and packaging), each program’s controls are different, leading to a wide variation of products across State-authorized programs. And the illicit marketplace is not subject to any standards or oversight. As a result, the range of products within the CSA’s definition of marijuana encompasses a large degree of variation in forms for consumption, composition of biologically relevant constituents, potency, and contaminants.” – Id. at 44606

As the DEA noted in the NPRM, “there is considerable variability in the cannabinoid concentrations and chemical constituency among marijuana samples and that the interpretation of clinical data related to marijuana is complicated.” Id. at 44607. Our expert testimony would address the following statement: “DEA anticipates that additional data on other marijuana constituents, routes of administration of marijuana, and the impact on D9-THC potency may be appropriate for consideration.” Id. at 44607. Since there are vast differences in the effects of marijuana based on THC levels and different methods of administration (e.g., smoking, vaping, dabbing, wax, edibles, etc.), our expert testimony and documentary evidence would provide further information on these points.

4. Its history and current pattern of abuse;

Consistent with the National Survey on Drug Use and Health (NSDUH) results from 2022, which were cited by HHS on page 44608 of the NPRM, we would provide expert testimony and documentary evidence to show the extensive and significantly increasing “use of marijuana for medical and nonmedical purposes”, admitted by HHS at page 44610.

With the DEA’s information from the World Health Organization (WHO) that “cannabis is globally the most commonly used psychoactive substance under international control ...[with] the global annual prevalence of cannabis consumption is 2.5 percent or about 147 million people” Id. at 44610, NDASA is concerned that the wrong conclusions are being drawn to permit rescheduling of marijuana. We would submit data and expert testimony to support the increasing trends referenced by DEA, when they quoted the WHO for data from the year 2016, when “an estimated 28.6 million individuals

age 12 or older were current (in the past month) illicit drug users.²⁴ By 2020, approximately 59.3 million individuals age 12 or older reported using an illicit drug within the past year; 83.6 percent (49.6 million) of those past-year illicit drug users reported using marijuana.” Id, at 44610. With the Domestic Cannabis Eradication and Suppression Program eradicating 4,435,859 illegally cultivated outdoor cannabis plants and 1,245,980 illegally cultivated indoor plants, totaling 5,681,839 illegally cultivated marijuana plants (Id. at 44610), NDASA remains concerned that the depth and breadth of the growth of illicit marijuana growing and production will not increased and not slowed by making marijuana a Schedule III drug.

As the DEA has requested, we would like to provide “additional data on marijuana’s pattern of abuse... appropriate for consideration in assessing this factor.” Id. 44610. NDASA would also like an opportunity to address the contradictory interpretation of the data by HHS in this, factor #4.

5. The scope, duration, and significance of abuse;

To address this, factor #5, “HHS analyzed the consequences over time of marijuana abuse compared to the abuse of other substances...” Id. at 44610. Their data actually indicates that the criteria for this factor was not met because the data provided in the NPRM showed marijuana is highly addictive, causes Substance Abuse Disorder (SUD), and that marijuana is the first or second most common drug for which people are admitted for in-patient treatment. Their facts simply do not support HHS’s conclusions on this factor.

Instead, in response to HHS's conclusions that other drugs were greater in the "scope, duration, and significance of abuse", DEA countered with their reasoning from their 2016 denial of a petition to reschedule marijuana to a Schedule III drug. "In 2016, DEA found that abuse of marijuana is widespread and significant. 81 FR 53739....DEA notes that national data demonstrate that marijuana is one of the most widely used federally illicit substances in the United States..." 89 FR 44613. As DEA requested, NDASA would like to provide expert testimony and documentary evidence to show "additional information regarding the scope, duration, and significance of marijuana abuse [that] may be appropriate for consideration in assessing this factor." *Id.*

6. What, if any, risk there is to the public health;

NDASA would like to provide evidence to contradict HHS's conclusion "that the risks to the public health posed by marijuana are low compared to other drugs of abuse (e.g., heroin (schedule I), cocaine (schedule II)), based on its evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and, most importantly, for overdose deaths." *Id.* at 44614

In apparent contradiction of the HHS's current conclusion on this factor, DEA noted its findings with HHS in 2016, when it was determined that:

[t]ogether with the health risks outlined in terms of pharmacological effects above, public health risks from acute use of marijuana include impaired psychomotor performance, impaired driving, and impaired performance on tests of learning and associative processes. Chronic use of marijuana poses a number of other risks to the public health including physical as well as psychological dependence." 81 FR 53739–40. (as noted at 99 FR 44614).

In response to this contradiction, NDASA would like to provide the expert testimony and documentary evidence requested by DEA in the form of “additional data on public safety risks, risks from acute and chronic marijuana use via oral and inhaled administration routes, and the impact of D9-THC potency may be appropriate for consideration.” 99 FR 44614.

The DEA correctly notes that studies have “examined the risk associated with marijuana use and driving”. Id. at 44614. NDASA would like to provide more insight into such data, including information from The Rocky Mountain High Intensity Drug Trafficking Area analyses and reports, which the DEA has cited. Id. at 44614. There are more studies and more information that should be analyzed before this factor can be decided in this rescheduling rulemaking.

7. Its psychic or physiological dependence liability;

Despite multiple sources of information showing psychic dependence and that marijuana was “the third most frequently reported primary substance of abuse, after alcohol (31.2 percent) and heroin (20.6 percent)”, Id. at 44614, HHS made a finding that this was not a sufficient concern to maintain the substance in Schedule I of the CSA. Id. at 44614. Similarly, with respect to psychological dependence, “HHS reported that up to 40 to 50 percent of individuals who use marijuana on a regular basis may experience physical dependence.” Id. at 44615. In fact, HHS concluded that it “found experimental and clinical evidence that chronic, but not acute, use of marijuana can produce both psychic and physical dependence in humans.” Id. at 44615

DEA referred back to its 2016 findings regarding long-term heavy use of marijuana as being likely to lead to physical and psychological dependence and that this dependence is underdiagnosed and undertreated in the medical setting. 81 FR 53740 and 99 FR 44615. NDASA would provide expert testimony and documentary evidence of additional information appropriate for consideration.

8. Whether the substance is an immediate precursor of a substance already controlled.

NDASA has nothing further to add on this point since “HHS concluded that marijuana is not an immediate precursor of another controlled substance. HHS Basis for Rec. at 61. This finding is consistent with DEA’s finding in 2016. 81 FR 53740.” 99 FR 44615.

VII. Determination of Appropriate Schedule for Marijuana

NDASA respectfully disagrees with the three findings HHS has made after conducting the eight-factor analysis above.

Specifically, we would offer expert testimony and documentary evidence to show marijuana continues to maintain the high potential for abuse that HHS and DEA found in 2016. Also, that the availability of marijuana and marijuana-derived products with extremely high levels of THC produce higher degrees of negative outcomes for the health of the individuals using marijuana and the safety of those around them.

NDASA would offer evidence to contradict the finding “that marijuana has a currently accepted medical use in the United States, specifically for the treatment of

anorexia related to a medical condition, nausea and vomiting (e.g., chemotherapy induced), and pain.” 99 FR at 44616. Pharmaceutically produced products (i.e., Marinol, Dronabinol) currently in Schedule III of the CSA meet this need. Yet, it is NDASA’s understanding that marijuana would not be dosed and dispensed by licensed pharmacists in the United States. In addition, NDASA would offer evidence into the record that both the WHO and the American Medical Association support research into determining whether marijuana has a legitimate medical purpose. For example, the AMA supports research in the area of using cannabis for medical purposes, but also has posted cautions for providers regarding encouraging the use of cannabis because of risks and the lack of research available. Based on the findings of one study, FDA has “found the available data indicated that there is some credible scientific support for the use of marijuana in the treatment of chronic pain, anorexia related to a medical condition, and nausea and vomiting, with varying degrees of support and consistency of findings. Additionally, no safety concerns were identified in FDA’s review that would indicate that medical use of marijuana poses unacceptably high safety risks...” Id. at 44619. NDASA would like the opportunity to offer evidence to the contrary.

III. State briefly the position of the person regarding the objections or issues.

Please see NDASA’s statements above regarding the matters upon which we would provide expert testimony and/or documentary evidence.

On a final but very important note, NDASA would like to provide expert testimony regarding reasonable alternatives to moving marijuana to Schedule III of the CSA. There are multiple options that are more factually supportable.

Assuming arguendo that the Attorney General and DEA would proceed with changing marijuana to Schedule III, NDASA would provide expert testimony as to the unintended and potentially catastrophic consequences to transportation safety and the need for a Safety Carve-Out through a simple but needed Executive Order.

All notices to be sent pursuant to the proceeding should be addressed to:

Jo McGuire, Executive Director
National Drug & Alcohol Screening Association
1629 K Street NW, Suite 300
Washington, DC 20006
Via email to: jomcguire@ndasa.com

June 16, 2024

Drug Enforcement Administration,

Attn: Administrator- DEA Federal Register Representative/DPW- Hearing Clerk/OALJ

8701 Morrisette Drive, Springfield, Virginia 22152.

Subject: Request for Hearing

Dear Sir:

The undersigned Panacea Plant Sciences C/O David Heldreth hereby requests a hearing in the matter of: DEA rule proposal: Schedules of Controlled Substances: Rescheduling of Marijuana also identified as Docket No. DEA-1362 and A.G. Order No. 5931-2024. (Previous hearing request mailed 6/14/2024 mislabeled the rule-making name/docket/order).

(1) state with particularity the interest of the person in the proceeding; (2) state with particularity the objections or issues concerning which the person desires to be heard; and (3) state briefly the position of the person with regard to the objections or issues.

Panacea Plant Sciences would like to verify standing in the rule-making by asserting that our company:

- 1.) is currently not licensed by the DEA.
- 2.) has research, IP and patent filings that incorporate marijuana, cannabis, THC and related items.
- 3.) PPS will be harmed if marijuana is moved into Schedule 3 instead of being de-scheduled and will be disadvantaged compared to those companies and businesses that have schedule 3 licensing. Rather than schedule 3, marijuana should be de-scheduled, in order to give PPS access.

Now in regards to the current rule-making, let us begin:

- A) To start there are apparent errors in the rulemaking process, in that the DEA did not consult with tribal governments as required under Executive Order 13175.

The rulemaking references active Executive Order 13175 - Consultation and Coordination with Indian Tribal Governments – however, it asserts that no such consultation with tribal governments is necessary, or as stated directly below:

"This proposed rule does not have tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes."

This statement is incorrect as this rulemaking will change the status of a substance under federal law from Schedule 1 to Schedule 3 it will then as such require changes to tribal law enforcement, tribal health care via independent or Indian Health Services, and other programs. Reservations are regulated as federal lands and many tribal law codes reference federal law and the Controlled

Substances Act. As such the current rulemaking will create a situation in which tribal governments and law enforcement will be required to train law enforcement on the new laws and this alone will impose direct costs on tribal entities and governments. Additionally, the costs of any enforcement of these new laws incurred from arrests, testing, jailing, etc. which falls on tribal governments again represent burdens and reasons for the DEA/Department of Justice to conduct a tribal consultation prior to rulemaking as is required under EO 13175. From the text:

"To the extent practicable and permitted by law, no agency shall promulgate any regulation that has tribal implications, that imposes substantial direct compliance costs on Indian tribal governments, and that is not required by statute, unless:

- (1) funds necessary to pay the direct costs incurred by the Indian tribal government or the tribe in complying with the regulation are provided by the Federal Government; or*
- (2) the agency, prior to the formal promulgation of the regulation,*
 - (A) consulted with tribal officials early in the process of developing the proposed regulation;*
 - (B) in a separately identified portion of the preamble to the regulation as it is to be issued in the Federal Register, provides to the Director of OMB a tribal summary impact statement, which consists of a description of the extent of the agency's prior consultation with tribal officials, a summary of the nature of their concerns and the agency's position supporting the need to issue the regulation, and a statement of the extent to which the concerns of tribal officials have been met; and*
 - (C) makes available to the Director of OMB any written communications submitted to the agency by tribal officials."*

Additionally, under the current DOJ tribal consultation policy, the DEA and DOJ are tasked to not narrowly define when it is necessary to consult tribal governments, but to do so in a way that is widely encompassing and to err on the side of consulting, rather than not. From the DOJ's own tribal consultation policy:

"The requirements of Executive Order 13175 and this Policy Statement generally will be construed liberally in favor of Consultation on any given policy as defined above with Tribal implications. Consultations may be organized in a variety of ways, from a single group discussion to a more iterative process involving a series of discussions. All decisions regarding whether and how to conduct a Consultation, or whether a given policy or topic has Tribal implications, will be coordinated with the Department's Office of Tribal Justice."

There are 574 federally recognized tribes and around 258 tribal law enforcement agencies. That is a large amount of affected tribal entities and a large impact. As such I ask that the DEA withdraw the current rulemaking and begin the mandated tribal consultation process under EO 13175 and DOJ's own policy. The DOJ policy also requires notice at least 30 days before the date of consultation.

As such Panacea Plant Sciences requests the rulemaking at hand be:

1. Withdrawn; and conduct tribal consultation which begins with a publication of notice seeking tribal input before rulemaking. The rule can be re-submitted for public comment and hearings after this is done.

B) The next issue at hand that must be dealt with is, the DEA's current rulemaking references the Regulatory Flexibility Act

Panacea Plant Sciences itself is a small business that qualifies under the Regulatory Flexibility Act to have consultation. PPS researches cannabis, does not have a DEA license, and has had to keep focus on hemp due to federal law, except when working with groups in other countries. Moving marijuana into schedule 3 from schedule 1, instead of de-scheduling will hurt PPS and give preferential treatment to those with DEA schedule 3 or other licenses.

There are hundreds to thousands of hemp farms that would qualify under similar circumstances. There are also universities and other entities which would qualify. As such there is ample reason to follow the Regulatory Flexibility Act.

From the Regulatory Flexibility Act:

"§ 602. Regulatory agenda

- (a) During the months of October and April of each year, each agency shall publish in the Federal Register a regulatory flexibility agenda which shall contain —*
 - (1) a brief description of the subject area of any rule which the agency expects to propose or promulgate which is likely to have a significant economic impact on a substantial number of small entities;*
 - (2) a summary of the nature of any such rule under consideration for each subject area listed in the agenda pursuant to paragraph (1), the objectives and legal basis for the issuance of the rule, and an approximate schedule for completing action on any rule for which the agency has issued a general notice of proposed rulemaking, and*
 - (3) the name and telephone number of an agency official knowledgeable concerning the items listed in paragraph (1).*
- (b) Each regulatory flexibility agenda shall be transmitted to the Chief Counsel for Advocacy of the Small Business Administration for comment, if any.*
- (c) Each agency shall endeavor to provide notice of each regulatory flexibility agenda to small entities or their representatives through direct notification or publication of the agenda in publications likely to be obtained by such small entities and shall invite comments upon each subject area on the agenda.*
- (d) Nothing in this section precludes an agency from considering or acting on any matter not included in a regulatory flexibility agenda, or requires an agency to consider or act on any matter listed in such agenda."*

We would like to let it be known that this rulemaking was not included on the DOJ or DEA Regulatory Flexibility Agenda. We would like the rulemaking withdrawn until this can be done.

As such Panacea Plant Sciences requests the rulemaking at hand be:

Withdrawn; and hold a small business and entity consultation which begins with a publication to that end prior to rulemaking in 2024 and potential final rulemaking in 2025.

C) Panacea Plant Sciences disagrees with the proposed placement of marijuana in Schedule 3, and instead finds that it should rather be removed from control completely and de-scheduled.

Although, international treaties may tie the United States to controlling marijuana, THC and other compounds; it is unlikely that this treaty violation will lead to any negative outcome. Canada has similarly moved to make marijuana a medicine and even went further to make it a regulated recreational item. There has been no backlash to this move and no consequences for them. As such the UN and the treaty parties are in effect silently complicit.

If marijuana is placed into a schedule, it should rather than schedule 3, be placed into schedule 5 due to its relative safety.

Additionally, cocaine was allowed as an unapproved by the FDA drug for medical use until 1919, when it was approved under branded formulations by several companies.

<https://www.fda.gov/drugs/unapproved-drugs/fda-notification-regarding-cocaine-hydrochloride-solution-products>

However, the allowance as an unapproved drug use, was via grandfathering, but that was on the principal that the cocaine was pure and always an exact item in the grandfathered drug formulations from prior to 1938. Cocaine is and was derived from a plant source, Erythroxylaceae coca, which produces several tropane alkaloids and other compounds. In fact, most cocaine is not pure cocaine, but rather a mixture of compounds extracted from the plant, unless chemically purified in a modern lab. This is important because there have been attempts to have marijuana allowed as a drug for medical use via the same grandfathering mechanism that allowed cocaine as an FDA unapproved drug to be used for medical use. However, the DEA/HHS/FDA denied that petition saying that they cannot verify the contents of the pre-1938 drug compounds as they are only labeled as marijuana flower or extract and not by compound (ie THC, CBD) However, again cocaine was allowed with unknown variation, but due to this same type of variation, this medical marijuana grandfather petition was denied.

<https://www.regulations.gov/document/FDA-2011-P-0671-0001>

This and the move to block wider access to cocaine for medical use, but instead only allow pharmaceutical branded approved versions, appear to be a move to consolidate the wider industry and supply of medicines into a small group of companies and people.

We make these points to argue that raw dried marijuana flower and marijuana/marijuana extract and/or tinctures should be allowed to be manufactured by DEA-licensed marijuana cultivators, manufacturers and compound pharmacies. Marijuana should then be allowed to be prescribed by doctors nationwide and filled by pharmacies.

Grandfathering (exempting from DEA/FDA regulation) state medical cannabis producers would also be a potential option.

Additionally, patients should be allowed to seek a prescription and if granted to seek a DEA license as a manufacturer and distributor/dispensary to cultivate/dispense their own medical cannabis, or to do so in a collective with other patients. Patients could also import from Canada if allowed.

The DEA is currently entering into agreements with religious organizations and churches to allow for their cultivation/importation and use of schedule 1 substances. If these smaller, non-commercial organizations are being allowed to have DEA licenses, then there is no reason why such a similar scheme could not be developed to provide access to the medical patients in the United States that wish to have immediate access, and to control their own supply of medication.

<https://www.marijuanamoment.net/federal-settlement-will-allow-arizona-church-to-import-process-and-use-ayahuasca-as-religious-sacrament/>

If the DEA, FDA, HHS and related agencies do not either, approve raw cannabis/extracts/tinctures as a FDA approved medication, provide a grandfather option via FDA/DEA as unapproved, but allowed medications, or allow state medical cannabis to be federally legal, then this rule-making does nothing to provide access to patients, and is effectively worthless except that providing 280E tax relief for federally illegal state medical cannabis businesses. There will be no reduction in costs or difficulty for research by this rule-making either, the only effective difference for research in schedule 1-3 is which box is checked on forms.

However, although marijuana as a botanical product and medicine may be safe, there are risks from marijuana and cannabis derivatives and products which has been seen in the public via the EVALI, lung injury vaping outbreak in 2020, 2,800 people were harmed and 68 died.

<https://www.yalemedicine.org/conditions/evali>

This outbreak primarily affected cannabis and hemp markets. One of the problems is the lack of regulations and the often lax regulations at the state levels. This leads to unregulated flavors/terpenes/cutting agents, from non-cannabis sources being added. For example vitamin e acetate, creating issues in the lungs with EVALI was cited

primarily via the acetate. However, companies in the hemp industry are now creating products with THC-O-Acetate that are inhaled, creating similar dangers.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9813278/>

Squalane was another large problem in Oregon, and other states. Squalane was sold by companies as a diluent.

<https://mjbizdaily.com/oregon-cannabis-regulators-ban-additives-first-seen-in-vaping-crisis/>

Mold and pesticides are also common in the state marijuana industry, and often under or un-reported. Testing is not done at the appropriate frequency and intensity for product safety. For example, Washington State only does pesticide testing of marijuana on random testing that takes years for every company to be tested. As such it took years for the state's marijuana regulator to find out that DDT derivative DDE had been identified in marijuana products, likely due to the farmland being used for other crops previously. A bulletin from the regulator on the issue can be found here: <https://content.govdelivery.com/accounts/WALCB/bulletins/36473ba>.

As such, PPS asks the government to regulate cannabis, hemp and marijuana products for safety, and use this rule-making to also apply the deeming rule under tobacco inhalation product rules to require the products to be held to the same standards of safety at a minimum if unscheduled.

However, if placed into Schedule 3, 4 or 5, due to the myriad problems with essentially, every state medical or recreational marijuana and hemp programs, PPS asks the government to regulate medical marijuana standards at a federal level so that the country has a consistent, fair, safe market for patients and business.

D) The DEA ALJ we believe is unconstitutional as similar ALJ schemes have been found so by the supreme court. As such we believe that this rule-making should if hearings are held, be heard instead of the ALJ in federal court. Also there are Chevron deference issues. These all likely are being addressed, while indirectly, in the Supreme Court via the Jarkesy v SEC lawsuit. As such we hold that the currently rule-making should be stayed until the Jarkesy ruling is final.

Further evidence and information will be presented in the future.

All notices to be sent pursuant to the proceeding should be addressed to:

Panacea Plant Sciences C/O David Heldreth

14321 Se 49th St

Bellevue WA 98006

Respectfully yours,



June 17, 2024

Drug Enforcement Administration, Attn: Administrator
8701 Morrisette Drive
Springfield, Virginia 22152

Subject: Request for Hearing

Dear Sir:

The undersigned, Bryn Spejcher, hereby requests a hearing in the matter of: Docket No. DEA-136. Transferring marijuana from Schedule I of the Controlled Substances Act ("CSA") to Schedule III of the CSA.

My name is Bryn Spejcher and I am a doctor of Audiology.

In December of 2023, I was convicted of involuntary manslaughter due to a tragic incident involving cannabis-induced psychosis which happened during Memorial Day weekend in 2018. The judge later sentenced me to three years' probation, with a condition to educate the public about the mental health harms and the dangerous risks of THC.

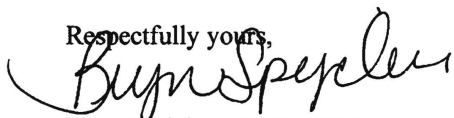
On behalf of Every Brain Matters, a nonprofit organization that is helping me fulfill my probation and public education outreach, I believe it is imperative for my voice to be heard in the critical discussions around the rescheduling of marijuana. I want to protect others from what happened to me and my late, deceased friend. Just like the majority of the population, I thought there were no harms in using marijuana. I was wrong.

As a novice user, my psychosis was purely the result of cannabis given to me by a regular, experienced user in the state of California, where marijuana is legal. During my criminal trial, the prosecutor's experts and my defense experts agreed this resulted in a cannabis-induced psychosis, and that I had no prior or post-incident mental health issues. This substance produced a severe psychotic reaction, something that is being seen more frequently around the world. My reaction produced a state of dissociation and detachment from the reality of my surroundings and cognitive processes, to the extreme, resulting in a tragic death and self-inflicting, permanent wounds.

I regret ingesting cannabis of any kind, now that I know the potential and serious risks of THC. Please consider my unforeseen, life-altering example.

All notices to be sent pursuant to the proceeding should be addressed to:
Bryn Spejcher
217 Edgebrook Drive
Bloomington, Illinois 60108

Respectfully yours,



Bryn Spejcher, Au.D., CCC-A, F-AAA
E: BSpejcher12@gmail.com

6/17/24

Date



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Littleton, CO 80123

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*Education and promoting effective laws to reduce Driving Under the Influence of
Drugs (DUID) – We provide a science-based perspective from DUID Victims.*

June 17, 2024

DEA Administrator
Drug Enforcement Administration
8707 Morrisette Drive
Springfield, VA
22151

Re: Docket No. DEA-1362

Dear DEA Administrator:

I request permission to testify at a hearing in opposition to the NPRM to downclassify marijuana.

There are many reasons the DOJ reclassification of marijuana to Schedule III should be rejected. The attached analyzes only one reason – the effects marijuana now has and its downclassification would have on the preventable tragedy of drugged driving deaths.

Attached is our position statement.

Sincerely,

A handwritten signature in blue ink that reads "Ed Wood".

Ed Wood
President, DUID Victim Voices

Enc: Traffic Safety Analysis of NPRM to Downclassify Marijuana

2024 JUN 21 PM 1:48

Traffic Safety Analysis of NPRM to Downclassify Marijuana

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Government regulators have abdicated their responsibility to consider traffic safety in their zeal to loosen the current barely existent restrictions on the commercialization of marijuana.

In making the case to deny the government proposal, DUID Victim Voices describes why the current preventable tragedy of drugged driving will only get worse if the DOI proposal is accepted.

UNTIL AN OBJECTIVE THC DRIVING IMPAIRMENT ASSESSMENT TOOL IS AVAILABLE, IT IS IRRESPONSIBLE TO DOWNSCHEDULE MARIJUANA. The danger to public safety of further support to the marijuana industry is too high without such a safety net in place.

Ed Wood
President, DUID Victim Voices
June, 2024

Summary

The DOJ/DEA/HHS analysis of the effect of marijuana's THC (Δ^9 -tetrahydrocannabinol) on driving safety is incomplete. It is shallow. It shows a complete lack of understanding of the data, the issues and the science of drugged driving. It is insulting to victims. It is incompetent. It would be a compliment to call it sophomoric.

DOJ, DEA and HHS have abandoned their responsibility to adequately assess the dangers to road safety of loosening restrictions on marijuana as proposed in the DOJ NPRM. It is irresponsible to even consider loosening restrictions without first understanding, communicating and dealing with the following issues of driving impairment caused by marijuana's THC:

- 1 The evidence of the dangers of THC-impaired driving to the public,
- 2 The ability (or lack thereof) of law enforcement agencies to enforce drugged driving laws, and
- 3 The impact of marijuana's downclassification on drugged driving dangers.

Regulatory agencies made no attempt to even acknowledge the above issues in the NPRM process.

Drugged driving, including THC-impaired driving is a deadly and growing problem. Whereas impaired driving was once just about alcohol, today only about half of DUI cases are due to just alcohol. The other half involve drugs. After alcohol, the primary drug causing DUI arrest and convictions is marijuana's THC. See page 16.

It was once difficult to prove that a driver was drunk and unsafe to drive, even in cases of crashes involving injury or death. Defense attorneys could plausibly claim, "It was an accident. It could have happened to anyone." The 1964 Grand Rapids Study demonstrated the correlation between blood alcohol content (BAC) and crashes¹. That study has been replicated with similar results many times by others^{2 3 4}. That quickly led countries around the world to adopt DUI *per se* laws that enable DUI convictions without proving impairment.

The effects of BAC *per se* laws have been impressive. DOT reported in 1968 that nearly one-half of traffic fatalities were due to alcohol. That percentage rose to 60% by the 1970s. Due to the adoption of BAC *per se* laws in the 1960s and the relentless campaigning by Mothers Against Drunk Driving founded by Candace Lightner, that percentage dropped to the 30% range by 1999 where it has hovered ever since. The drop is even more impressive when one realizes that the base number of traffic fatalities dropped at the same time, likely due to improvements in automobile and highway design.

There is no THC analog to alcohol's ubiquitous BAC *per se* level. Some jurisdictions have adopted THC *per se* or permissible inference laws, but none of those laws are based on scientific evidence as alcohol legal limits are. There is no scientific evidence supporting THC *per se* levels. It is not because we haven't found the proper level yet, it is because the "right" level does not exist. It can't. The chemistry and pharmacokinetics of THC prohibit the correlation between blood THC levels and crash risk that exists for alcohol.

Law enforcement agencies struggle with drugged driving, as they did with alcohol prior to the implementation of *per se* laws. Families of drugged driving victims pay the price of this problem every day. Perhaps someday technology will be developed akin to a Star Trek Tricorder that can determine if someone is impaired. But that technology will not be based on blood THC levels because we know that will not work.

UNTIL AN OBJECTIVE THC DRIVING IMPAIRMENT ASSESSMENT TOOL IS AVAILABLE, IT IS IRRESPONSIBLE TO DOWNSCHEDULE MARIJUANA. The danger to public safety of further support to the marijuana industry is too high without such a safety net in place.

The proposed downclassification of marijuana would encourage more use of marijuana which will pose a danger to both users and to the non-using public, as past drug liberalization policies have. The result will be more auto crashes, many fatal. Lacking a valid THC driving impairment assessment technology, legislatures will continue to adopt flawed THC *per se* or permissible inference limits that will make it even more difficult to convict THC-impaired drivers who test below the limit. Colorado's experience proves that to be the case⁵.

Major policy decisions should not be made lightly. They should be based on rigorous data analysis and an understanding of the relevant science and data. Efforts should be made to fill in known knowledge gaps before making major policy decisions, especially decisions that that could make matters worse. One reason for DOJ's specious arguments in favor of rescheduling is a lack of readily available and reliable data on the actual causes and consequences of impaired driving.

STATES SHOULD BE INCENTIVIZED TO COLLECT AND PUBLISH DATA ON THE CAUSES AND CONSEQUENCES OF IMPAIRED DRIVING. Colorado's effort described on pages 16-19 is by no means perfect, but it is a model upon which other states can begin to build.

Failings of HHS/DEA/DOJ analyses

Both HHS and DEA recognized that traffic safety is a legitimate concern when considering marijuana policies by the fact they mentioned it in their analyses. But that's all they did.

HHS didn't even try to deal with the drugged driving issue. HHS devoted three paragraphs to drugged driving in its 252-page letter to the DEA⁶. They simply reported results of two surveys on the self-reported prevalence of drugged driving. One from NSDUH - the National Survey on Drug Use and Health, and the other from YRBSS - the Youth Risk Behavior Surveillance System. That was their entire analysis.

DEA did a little bit better. Its single paragraph on drugged driving in the NPRM⁷ inaccurately reported two largely irrelevant epidemiological studies purporting to show the growing threat of fatalities from THC-impaired driving.

The first report was the Volume 8 study of The Effects of Marijuana Legalization from the Rocky Mountain High Intensity Drug Trafficking Area (RMHIDTA)⁸. The report showed that Colorado fatal crashes where the driver tested positive for marijuana more than doubled between 2013 and 2020, from 55 to 131, based on data from coroners statewide. The report did not differentiate in its “tested positive for marijuana” category, the difference between psychoactive THC and its inactive metabolite 11-nor-9 Carboxy-THC. Early data included cases positive for the inactive metabolite only. Therefore, the number of crashes where the driver was positive for psychoactive THC in 2013 was likely lower than 55. By 2020, the data sources had improved to report only the psychoactive drug. The increase in fatalities was therefore even worse than shown.

DEA cautioned however, that “other evidence in the same report suggests that DUI citations involving marijuana have grown at a rate similar to the rate for citations involving other drugs.” Whereas the first RMHIDTA claim was backed by toxicology reports from statewide coroners, the second claim was only from the Colorado State Patrol, based on opinions of arresting officers, with no toxicology confirmation. While State Patrol evidence is of interest, the two evidence measures are hardly comparable.

The second report was the Public Health report from Wilson in 2014⁹ showing, according to the DEA, that “among drivers who test positive for at least one drug in a traffic stop, a growing share test positive for cannabis.” The DEA report is incorrect. Forensic toxicology laboratories do not and cannot test for cannabis or marijuana. They test for the impairing chemical delta 9-tetrahydrocannabinol, aka THC. Wilson’s data came not from traffic stops, but from the Fatality Analysis Reporting System (FARS), sponsored by the National Highway Traffic Safety Administration (NHTSA).

The biggest problem with the Public Health report is that FARS was designed to capture data on drunk driving, not drugged driving. FARS does an excellent job reporting drunk driving data, but a poor job in collecting drugged driving data. There is no standardization of drug testing and reporting from state to state or even from year to year within a state as there is with alcohol testing and reporting. Because of that, in 2014 NHTSA advised against using FARS data to infer anything about drugged driving comparisons from state to state or from year to year¹⁰.

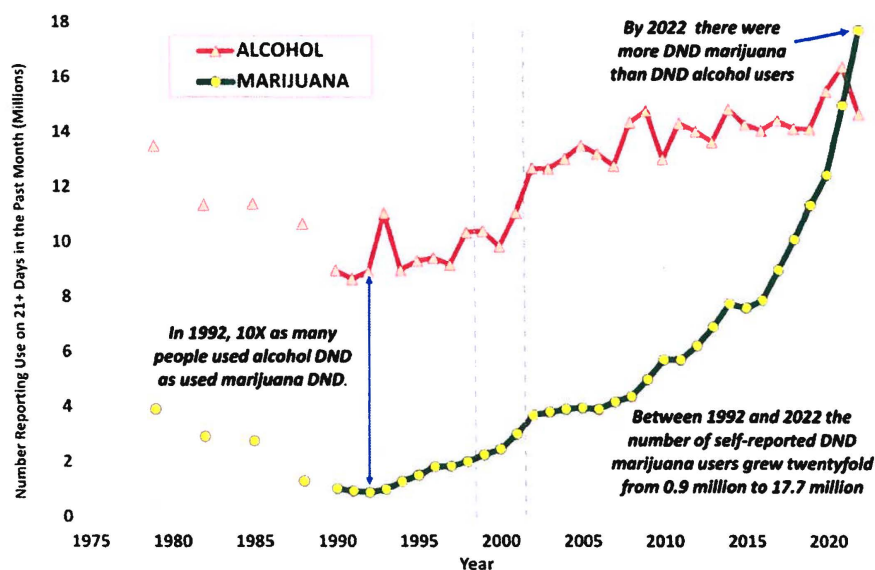
Even more fundamentally, both reports suffer from the same major flaw that render their conclusions somewhat irrelevant. Both reports are based on measurements of drug presence, not of drug impairment. If there were a strong proven correlation between drug presence and drug impairment, the reports would have more value. But lacking such a correlation, the reports are largely irrelevant. There are studies that are much more relevant. See Pages 10-19.

During the time windows of the two DEA-covered reports, the number of Daily and Near Daily (DND) marijuana users rose dramatically¹¹. In 1971, the federal government established the White House Drug Office in response to an increase in illicit drug use nationally, adding new demand reduction efforts to the long-established supply reduction policies. DND marijuana use was increasing, peaking in the late 1970s. See Figure 1. The

Atlanta-based Parent Movement focused on reducing youth marijuana use and subsequently led Nancy Reagan to introduce the “Just Say No” slogan nationally in 1981. Youth marijuana use declined to a low in the early 1990s, and nationally, DND marijuana use declined by about 75%. Then in 1996, California legalized the medical use of marijuana. The Federal Government’s lack of response to California’s ignoring Federal law was an effective surrender in the War on Drugs. After the federal surrender in the 1990s, DND use rose dramatically, first accelerated with the 2009 Ogden Memo¹², and then even more as recreational marijuana shops began opening in 2014. Between 1992 and 2022 the number of self-reported DND marijuana users grew twentyfold from 0.9 million to 17.7 million. Policies have an impact.

Since DND users may test positive for THC long after consumption (See #4 on page 9), the findings of both studies reported by DEA/DOJ could have occurred even if THC had no effect whatsoever on driving skills.

Figure 1 – Changes in self-reported marijuana use in the United States from 1979 to 2022



Addiction, First published: 22 May 2024, DOI: (10.1111/add.16519)

None of the agencies wrote about the abundant experimental or epidemiological evidence proving that THC can and does impair driving skills, leading to crashes, some of which are fatal. None talked about the magnitude of the danger to the public. Victims were neither mentioned nor recognized. There was no discussion of how prohibitions on drugged driving are enforced in DUI laws from state to state, or why the primary tool used to enforce drunk driving laws (Blood Alcohol Level) does not have an analog that could be used to enforce drugged driving laws. The possible effects on highway safety of downclassifying marijuana was ignored.

Why do blood THC levels and THC impairment levels not correlate?

Why should anyone expect them to correlate? THC does not impair a person's blood. Neither does alcohol. Neither drug impairs human blood. Both drugs impair the human brain, not the blood. But since alcohol is water-soluble and THC is fat soluble, that's where the similarity ends¹³.

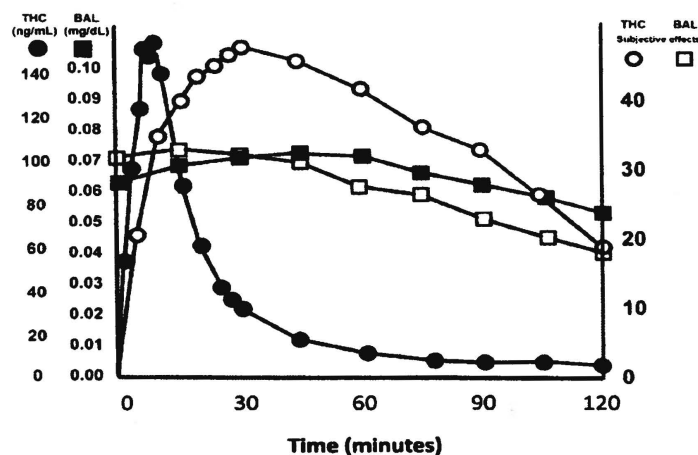
1 THC blood levels do not represent levels of THC in the impaired brain.

Being a water-soluble molecule, alcohol quickly establishes a uniform concentration across highly perfused organs and tissues. That means that what's in the brain is in the blood and vice versa. We can test the alcohol content in a subject's blood as a surrogate to make a very good estimate of what's in the subject's brain.

That cannot happen with THC. THC is a fat-soluble molecule that is insoluble in blood, although it can be entrained in blood like sand in a muddy river. Instead of remaining dissolved in blood, THC is quickly absorbed by the brain and other fatty tissues. The maximum blood level of THC drops an average of 79% within the first 25 minutes after beginning to smoke a joint¹⁴.

A user's blood THC level rises very rapidly upon initiation of smoking, peaking in typically less than eight minutes. Then the THC level drops almost as rapidly while the brain and other highly perfused fatty tissues and organs clear the THC from the blood. Both a subjective sense of being high and impairment begin to rise as the brain absorbs THC – even while the THC level in the blood is dropping! See Figure 2. There is a brief period during the first hour after beginning to smoke a joint when the blood THC level approximates the brain THC level. Otherwise, sometimes one is going up while the other is going down.

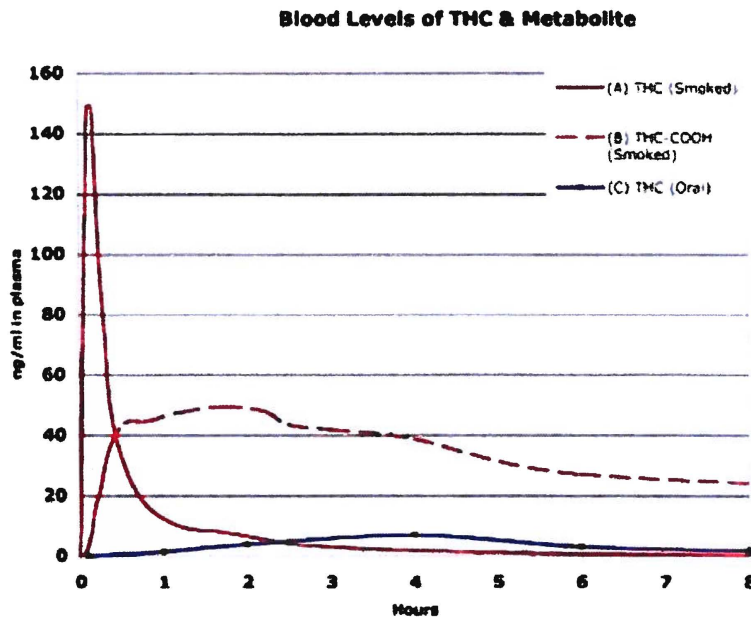
Figure 2 Blood levels of alcohol and THC compared with subjective effects



Source: American Journal of Addiction (2009)¹⁵

After a user's smoking session has ended, THC continues its redistribution from the blood to fatty tissues and organs. THC is slowly metabolized to the psychoactive 11-Hydroxy-THC which in turn is quickly metabolized to the non-psychoactive secondary metabolite 11-nor-9-Carboxy-THC. Carboxy-THC is water soluble, so it will remain in the blood until it is metabolized and excreted, long after psychoactive THC can no longer be detected. The typical THC concentration is shown in the solid red line in Figure 3. Carboxy-THC is shown in the dashed red line in the same figure. The solid blue line showing blood THC levels for orally consumed marijuana shows that THC consumed orally behaves far differently than smoked or vaped marijuana [See more on page 9]. THC from marijuana consumed orally does not create a high level in blood as inhaled THC does, blood levels peak later than inhaled THC, and its effects start much later and last much longer than inhaled THC.

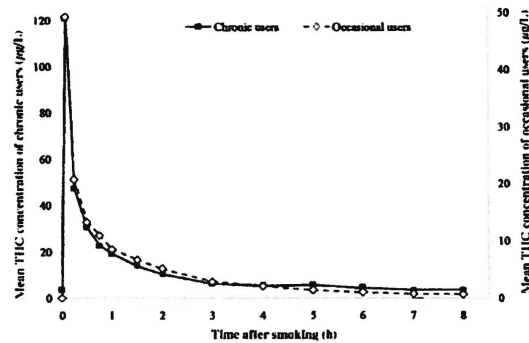
Figure 3 Blood Levels of THC and Carboxy-THC



Source: Drawn from data in Huestis et al. 1992¹⁶

The THC concentrations shown on Figure 3 represent averages of a group of subjects. The actual number varies widely by individual and by user experience. Figure 4 shows the THC clearance from blood from two groups of users – chronic users and occasional users¹⁷. Two different y-axes are used to normalize scaling, showing equal height for both chronic and occasional users. Chronic users consume a much higher dose than occasional users, resulting in a higher maximum blood THC level. But the clearance profile from blood is identical in both groups.

Figure 4 Toennes redistribution curve

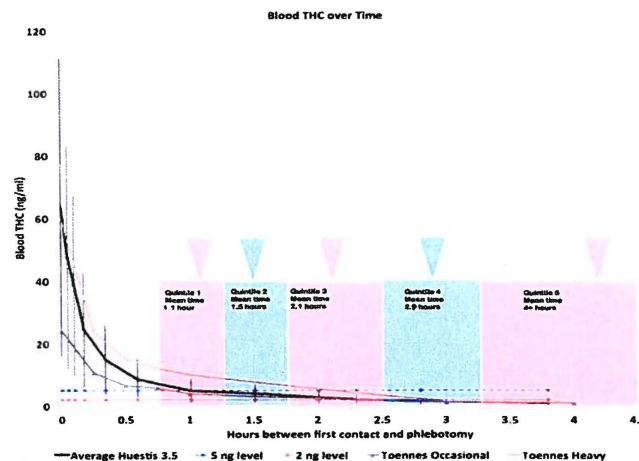


Source: J Analytical Toxicology, Sept 2008

The average time between an arrest and the time a blood sample is collected for testing is about an hour¹⁸, two hours if there is a death or injury crash involved, and three hours if a warrant is required to obtain a blood sample¹⁹. Because of these normal delays in time to collect a blood sample, in some cases, the blood THC level can be below laboratory detectable levels even if the driver was smoking marijuana at the time of DUI arrest or a crash.

Figure 5²⁰ shows data from Figures 3 and 4 on a single y-axis, rescaled to show concentration of THC in nanograms per milliliter (ng/mL) of blood, rather than in serum or plasma. It also shows times from a crash until blood was collected in cases of vehicular homicide or assault, by quintiles. The mean of the 3rd quintile of 2.1 hours shows that for a driver smoking a joint at the time of a crash, the blood THC level would be between 2 and 5 ng/mL of blood, depending on the user's experience with THC use.

Figure 5 – Test delay quintiles overlaid on THC redistribution curves



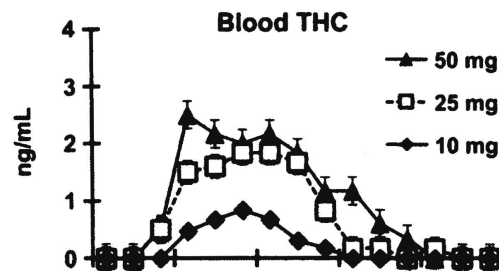
Source: Traffic Injury Prevention, May 2015

The terminal half-life of THC in the human body is about 4 days²¹. THC remains in the body, either bound to CB1 or CB2 receptors, or dissolved in interstitial fat and other fat reserves long after THC can no longer be detected in blood. In a series of autopsy studies, Mura found that the concentration of THC was higher in 100% of his subjects' brains than in their blood. In some cases, he found high levels of THC in brain tissue when none could be detected in blood²².

2 THC in edibles behaves differently than inhaled THC.

THC edibles do not generate the high blood THC levels that inhaled THC products do. This is because orally consumed THC undergoes hepatic metabolism before entering the bloodstream. Smoking or vaping marijuana injects a huge bolus of THC directly into the bloodstream via the lungs. This was shown on Figure 3, but the detail for the THC concentration from orally consumed marijuana could not be readily quantified due to the graph scaling. That detail can be seen more clearly from Vandry's multicenter study²³ of the pharmacokinetics and pharmacodynamics of orally consumed THC. See Figure 6. For a normal 10 mg dose, the maximum THC concentration in blood was less than 1 ng/mL. That level can be measured in some research laboratories, but 1 ng/mL is the lowest reporting level (Limit of Quantification) for most forensic toxicology laboratories. The maximum THC concentration was less than 3 ng/mL for subjects consuming five times the normal 10 mg dose.

Figure 6 Blood THC level vs time since oral consumption



Source: J Analytical toxicology, March 2017

3 Chronic users can be less affected by THC than novice or occasional users.

To maintain homeostasis, the body of a chronic marijuana user downregulates the quantity of CB1 receptors in the brain^{24 25}. This provides a level of tolerance to some, but not all of the impairing effects of THC. Early studies²⁶ found that chronic marijuana users had a partial tolerance to the psychomotor impairment of THC. Later studies^{27 28} have modified those conclusions somewhat, finding that a chronic user exhibits some tolerance for cognitive impairment, but less so for other impairment domains.

4 Chronic users can have high blood THC when not acutely impaired.

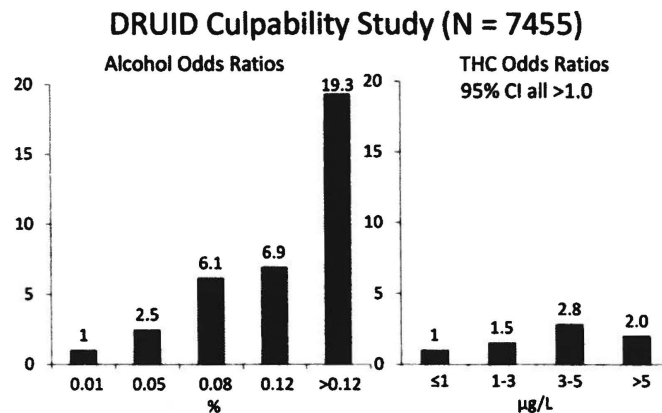
Chronic users claim that they may have elevated THC blood levels even when they are not acutely impaired. There is a good reason for this. Fat cells in the body are not an infinite

sink for THC. As fat stores become saturated with THC, some THC is released back into the bloodstream. Consequently, chronic users can maintain a measurable level of THC in their blood long after acute impairment has subsided²⁹.

5 Epidemiological evidence confirms the lack of correlation.

As noted above, several researchers have studied the effect of BAC on crash risk. But the lack of correlation between crash risk and THC blood levels is well known. Therefore, analogous THC studies of crash risk have typically analyzed crash risk as a function of a dichotomous variable – the presence or absence of THC – rather than as a function of THC blood levels. An exception is the multi-country European DRUID study³⁰ which mimicked the crash risk correlation for drunk driving, but ended up confirming that there was no correlation between blood THC levels and crash risk. See Figure 7.

Fig 7 – Crash risk of alcohol vs THC impaired drivers



Evidence that THC impairs driving

The weakness of evidence in the HHS/DEA/DOJ analyses does not mean the evidence is weak for THC's role in causing driving impairment. Some evidence was given in the NPRM's 8-factor analysis – Pharmacological effects. More evidence specifically relevant to safe driving is abundant and falls into the following categories:

Experimental evidence

1. Laboratory experiments
2. On-road driving studies
3. Driving simulator studies

Epidemiological evidence

4. Case control studies
5. Culpability studies
6. Observational studies

1 Laboratory experiments

These are the most rigorous types of experiments to prove impairment. They are comparatively easy and inexpensive to perform. They are highly controlled and have reproducible results. Because of the nature of laboratory experiments, they cannot fully represent the many marijuana cultivars, THC concentrations or modes of administration used in the real world. They conclusively prove that THC can cause impairment of driving skills but have been criticized by those who claim that proof of laboratory impairment does not prove that THC impairment causes danger to highway users.

Sewell's 2009 review of cognitive studies³¹ of the effects of marijuana noted impairment of attentiveness, vigilance, perception of time and speed, and executive function. Impairment is prominently found in tasks requiring divided attention. When used together with alcohol, the impairing effects of the two drugs are at least additive and possibly multiplicative, which may depend upon the impairment dimension being assessed.

The National Safety Council concluded³² that acute THC intoxication produces dose-related impairment in cognitive and psychomotor functions as well as risk-taking behavior. THC also alters reaction time, short-term memory and attention, motor skills and tracking, all of which can impair driving skills.

A most helpful report on this topic is Solowij's systematic review of 105 experimental studies of the effect of THC on cognition³³. Results were summarized by primary cognitive domain in order of evidential strength for both acute and chronic exposure. Where data were available, the persistence of impairment of chronic users after abstinence was reported.

Solowij found strong and largely consistent evidence that THC impaired focused, divided and sustained attention for both chronic and occasional users regardless of sex. After an acute impairment episode, residual chronic impairment in chronic users gradually subsided over a period of several weeks of abstinence. There was also strong and largely consistent evidence that THC impaired psychomotor function acutely, but the evidence was weaker for similar impairment of chronic users of marijuana. Impairment likely persists during abstinence after chronic use, but the data are mixed. Executive function impairment studies produced mixed results with a tendency to see greater impairment in older subjects with a long history of chronic THC use, indicating a perturbed development of the frontal lobes.

2 On-road driving studies

There are few studies of this type due to their danger, expense, and difficulty in ensuring rigor. For safety considerations, doses of THC have been relatively low in this type of study.

Huestis reviewed three Dutch studies, all on young occasional cannabis users³⁴. Two of the studies demonstrated a strong dose-response effect of THC consumption on SDLP (Standard Deviation of Linear Positioning). The third study used a low 100 µgm/Kg dose of THC (approximately 7 mg, or one-third of a joint made with 5% THC marijuana) and found

no effect on outcome measures. Other than journalistic publicity stunts, there have been no other recently published on-road driving experiments.

3 Driving simulator studies

These studies can be well-controlled and result in highly credible results. This is the best way to deal with the fact that laboratory experiments do not directly measure the effect of THC on traffic safety. Expense and logistical considerations confine these studies to a limited number of participants compared with epidemiological studies. Simulator studies measure fewer dimensions of impairment than are possible with laboratory studies. An unverified concern with driving simulator studies is that the drivers are fully aware that they are being monitored. Therefore, the tests may simply assess how subjects can drive rather than how they do drive.

Huestis noted³⁵ that simulators permit measurement of driving performance aspects that cannot be achieved with actual road-driving experiments. Her research team reviewed nine simulator studies, two of which studied the effects of THC and alcohol. None evaluated chronic marijuana users. Study designs varied, with reaction time, tracking, speed and speed variation being the most commonly measured of the ten domains reported in the review. There were inconsistent results in half of the domains tested but eight of the nine studies reported impairment in at least one domain. SDLP, a measure of weaving in the lane, was the most sensitive road-tracking measure with two of four studies showing a THC-associated impairment.

After reviewing prior work, the Huestis team studied the impact of THC concentrations with and without alcohol using a highly instrumented simulator on 18 occasional marijuana users using vaporized marijuana³⁶. That study found that 8.2 ng/ml of THC in whole blood provided a similar SDLP to an alcohol level of .05 gm/dL. Huestis cautioned that her interpolated THC concentrations at the time of impairment measurement were not representative of forensically determined THC levels due to the rapid redistribution of THC from the blood immediately post-dosing. The study found that the effects of THC and alcohol on SDLP were additive, rather than synergistic.

Brooks-Russell compared simulator performance of occasional and daily marijuana users who smoked their chosen THC product at their chosen dose³⁷. Daily users consumed a higher THC dose than occasional users, as similar studies have found. Occasional users had higher impairment levels than daily users as measured by SDLP. Daily users had a higher decrement in speed than occasional users.

Marcotte³⁸ found that regular users had much lower Composite Drive Scores (CDS) at ½ hr and 1½ hr post smoking, and moderately lower CDS at 3½ hrs. Most CDS decrements were fully resolved at 4½ hrs post smoking. Most subjects felt unsafe to drive immediately after dosing. Most felt safe to drive at 1½ hrs even though their CDSs had not improved since their immediate post-dosing assessment.

Although Marcotte found that most CDS decrements were fully resolved at 4½ hours after smoking, others have reported chronic impairment continues for chronic users well after acute impairment has subsided^{39 40 41}.

The effect of chronic impairment (as opposed to acute impairment) on driving safety has not been determined, but an Australian study found impairment on an aviation simulator 24 hours after consumption⁴².

4. Case control studies

These epidemiological studies compare drivers in crashes with similar drivers who were not involved in crashes. It is essential to establish a valid control group for these studies to have high value. Outcomes of these studies are typically Odds Ratios (ORs), or crash risks relative to sober drivers. There have been literally thousands of such study reports of varying quality. Fortunately, several meta-analyses ease navigation through these numerous, often conflicting studies.

Li's 2011 meta-analysis⁴³ selected 9 studies out of a total surveyed population of 2,960 published reports. The nine were selected based on quality and sufficient comparability to enable a high-quality meta-analysis. His meta-analysis totaled 4,236 cases and 88,993 controls and focused on marijuana use rather than THC presence. The most common source of exposure data were self-reports or urine tests, followed by blood tests. All but one study reported a significant risk to driving safety with marijuana use. The estimated summary OR was 2.66 (2.07, 3.41) for a fatal crash from marijuana use.

Asbridge's similar meta-analysis⁴⁴ published a few months later had similar results, yielding an OR of 1.92 (1.35, 2.73). His most common source of THC exposure in studies selected for analysis was blood or serum assays rather than self-reports or urine analysis.

These studies led to a commonly accepted view that the OR of a fatal crash from marijuana use was about 2. Five years later Rogeberg critiqued and re-evaluated both studies and then performed his own meta-analysis, finding ORs to be 1.36 or 1.22, depending on the analytical technique used.

One dilemma with the above case control studies is their reliance on THC presence or use, rather than THC impairment to assess the crash risk. As noted above, THC presence bears little relevance to THC impairment.

Some falsely claim that the 2016 NHTSA-sponsored Virginia Beach case control study found that there is no link between marijuana use and crash risk. The truth is that the authors did not find there was no link; they failed to find a link. Absence of proof is not proof of absence. They also failed to find a link between crashes and any other drug or drug combination other than alcohol. The link found between alcohol use and crash risk was about half what legacy studies from Borkenstein, Krüger, Zador and Blomberg found. NHTSA's study design was badly flawed. Not all study subjects were included in the analysis; only those who volunteered were included. The sample size was too small to find a statistically significant link for any drug other than alcohol. At least 413 of the 3,095

subjects tested were not the crash initiator, but innocent victims who were involved in a crash. The study consisted of mostly “fender bender” crashes. There were only 15 fatal crashes out of the 2,682 studied. The study was conducted on secondary streets. High speed highways were excluded. The study site had a lower drug use (14.4%) than the national average (19-22%). The study concluded, “This study should not be interpreted to mean that it is safe for individuals who have used substances to operate a vehicle.”

5. Culpability studies

These studies examine drug presence in fatal and/or crash cases, comparing data from culpable drivers and non-culpable drivers. Outcomes of these studies are typically Odds Ratios, or risk relative to sober drivers.

Culpability studies of large populations have not unequivocally answered the question of the role of marijuana in traffic crashes, in part due to the wide variations in study design. Below we discuss only studies using blood testing and with two exceptions, those that distinguished THC from its inactive metabolite Carboxy-THC. All studies found an effect of marijuana on crash risk.

Longo’s 2000 study⁴⁵ involved 2,500 injured and deceased drivers tested for alcohol, THC, benzodiazepines and stimulants. Drivers were determined to be either culpable or non-culpable. The 6.2% whose culpability was only contributory were not included in the study. Drug- and alcohol-free drivers were culpable in 52.5% of the cases, THC-positive drivers were culpable 47.5% of the cases indicating no significant marijuana involvement. However, there were only 44 drivers found with THC *only* and those with a THC level at or above 2 ng/ml were culpable 66.7% of the time, indicating significant marijuana involvement. The time interval between crash and taking of a blood sample was not reported.

Drummer’s 2004 study⁴⁶ involved 3,398 fatal crashes, including 59 whose drivers tested positive for THC *only*. Drummer excluded drivers from his study whose culpability was only contributory. He found an odds ratio (OR) of 2.7 for being involved in a fatal crash if the driver was positive for THC, and 6.6 if the driver had a blood THC level above 5 ng/ml. In comparison, the OR for alcohol-positive drivers was 6.0 and 17.4 if both alcohol and THC were present. This is one of the few published studies showing different ORs at different blood THC levels. This may be due to the source of the data (shock trauma setting rather than law enforcement arrests), or due to the low number of cases positive for THC *only*.

Similar studies by Laumon⁴⁷, Bédard⁴⁸, and Li⁴⁹ resulted in OR findings between 1.39 and 1.82 for THC-positive drivers.

These culpability epidemiological studies show, albeit inconsistently, that drivers positive for THC were more likely to cause fatal crashes than drivers not positive for THC. The increased risk to the driving public caused by marijuana-using drivers is measurable, but less than the risk caused by drunk drivers. However, when the two substances are combined, the risk is greater than the risk caused by either drug alone. In studies that

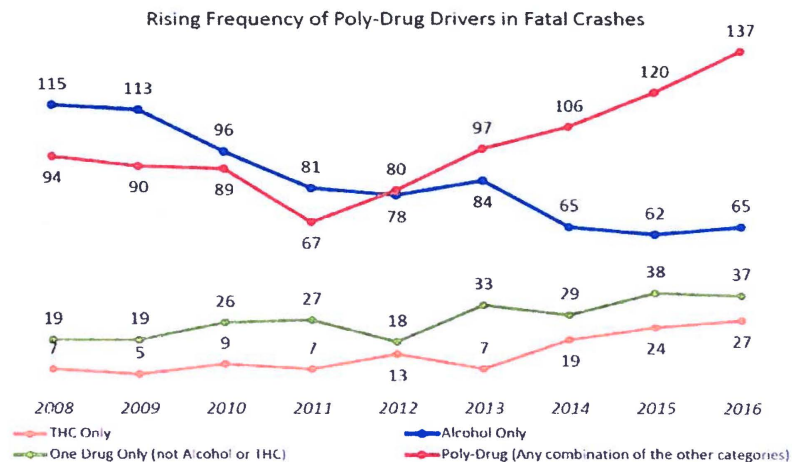
evaluated drivers' use of alcohol and marijuana, more drivers were found using both drugs than were found using marijuana alone.

6. Observational studies

The two reports described by the DEA are examples of observational reports and suffer from the criticisms described above: use of a flawed FARS data source, and reliance on drug presence rather than drug impairment. Outcomes of these studies are typically trend graphs and comparative ratio reports. Generally, they are helpful but not often dispositive.

Here is another observational study that may be more instructive than those cited by DEA/DOJ. The state of Washington opened its first retail marijuana sales store in July 2014. The state has had a fairly stable 60% testing rate for both drugs and alcohol of drivers in fatal crashes from 2008 to 2016. The Washington Traffic Safety Commission has an excellent record of reporting toxicology results of drivers involved in fatal crashes using data from the Washington State Patrol Crime Laboratory Division. Some results are shown in Figures 8. Although toxicology tests indicated an increase in THC-positive drivers like the cannabinoid-positive drivers from the Colorado report below, the more significant concern in Washington was polydrug-positive drivers, most of which were cannabinoid and alcohol positive⁵⁰.

Figure 8 – Washington State crash fatalities 2008-2016



Source: Grondel, Washington Traffic Safety Commission Apr 2018

Several other observational studies compared traffic deaths per billion vehicle miles traveled (BVMt) in states that have commercialized the sale of recreational marijuana with those that have not. It appears that the problem may be getting worse.

Aydelotte's 2019 study⁵¹ found that states with commercial marijuana sales had 1.9 more deaths per BVMt than states that did not.

Kamer's 2020 study⁵² found that states with commercial marijuana sales had 2.1 more deaths per BVMT than states that did not.

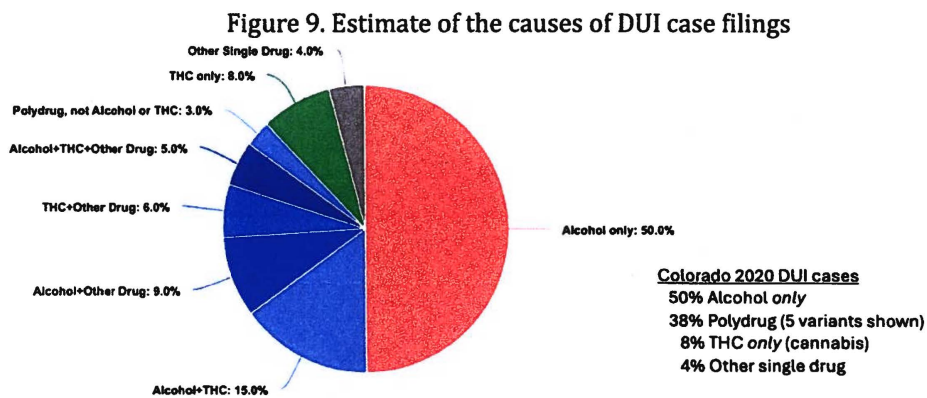
Adikari's 2023 study⁵³ found that states with commercial marijuana sales had 2.22 more deaths per BVMT than states that did not.

These studies translate into a projected 6,000 additional annual deaths if all states were to commercialize marijuana. None of the above studies relied on drug test results from FARS. The reported increased death rates are consistent with the overall traffic death rate increase during the last decade published by the Department of Transportation⁵⁴.

Unique Colorado observational studies

In 2007 Colorado enacted C.R.S 24-33.5-520, a law requiring the Office of Research and Statistics (ORS) in the Division of Criminal Justice of the Division of Public Safety to annually publish a report on the causes and judicial consequences of DUI in the state. The analysis authorized ORS to combine the data of toxicology laboratories and evidentiary breath testing with the data of state judicial to determine which drug or drugs were responsible for each DUI offense.

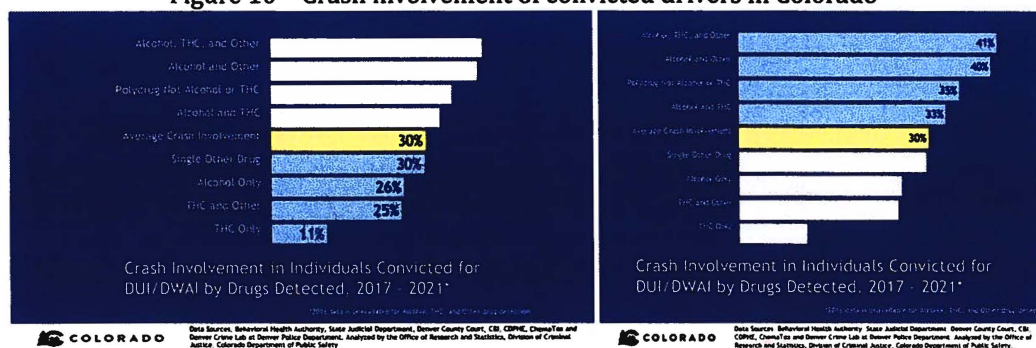
The effect of the law was to provide the state with data on not just drug presence, but on court-determined drug impairment. We can now provide a reliable estimate on the prevalence of drugs in DUI case filings, shown in Figure 9.



Source: <https://www.duidvictimvoices.org/how-common-is-drugged-driving/>

We also now know that driving under the influence of THC *only* was about 42% as dangerous as driving under the influence of alcohol *only* as shown in Figure 10, which shows crashes in those convicted of DUI in various drug categories. Driving under the influence of both THC and alcohol was 27% more dangerous than driving under the influence of alcohol *only*.

Figure 10 – Crash involvement of convicted drivers in Colorado



Source: Rosenthal, Lifesavers Conference April 2024

For context, it should be noted that the average BAC for alcohol *only* drivers during 2017-2021 was 0.16. That corresponds with a crash risk 29.48 times higher than a sober driver, according to Bloomberg's crash risk analysis⁵⁵.

We can now estimate that the crash risk of drivers convicted of driving under the influence of THC *only* was about 12 times that of a sober driver ($29.48 \times 42\%$) and that a driver convicted of driving under the influence of both THC and alcohol had a crash risk over 37 times that of a sober driver. These estimates should stand on their own, and not be compared with the crash risk results of the epidemiological studies described above. Earlier studies measured crash risk as a function of THC presence. The above shows crash risk as a function of THC impairment.

C.R.S. 24-33.5-520 also provides the state with an understanding of how effectively it is enforcing DUI laws as a function of the substance causing the impairment. All data here are from the August 2023 Colorado report⁵⁶.

Alcohol <i>only</i>	94%
Polydrug	87%
Other single drug	79%
THC <i>only</i>	75%

These are three-year averages for 2018-2020

This includes findings of Guilty, Deferred and Deferred/Dismissed

This combines convictions for DUI and DWAI

The comparatively low conviction rate for drivers impaired by single drugs other than alcohol is despite Colorado have a highly capable and dedicated Colorado Transportation Safety Resource Prosecutor and a 5 ng/mL THC permissible inference law that was intended to improve THC impairment convictions.

Colorado has several unique features of its DUI law:

1. There are two offenses. The higher offense is DUI. The lower offense is DWAI (Driving While Ability Impaired).
2. DUI is defined as incapable of safe driving. DWAI is defined as impaired to the slightest degree so the person is less able to drive safely.
3. The 5 ng/mL THC permissible inference law applies to DUI, but not to DWAI.
4. Administrative sanctions are lower for DWAI, but both offenses have identical criminal sanctions (except lower sanctions for the first DWAI offense).

Although THC *only* convictions for THC *only* are 75%, the convictions vary by offense and THC blood level. THC *only* convictions for DUI were 46% and convictions for DWAI were 99%, both irrespective of the blood THC level.

Further analysis reveals:

		DUI	DWAI
Alcohol <i>only</i>			
	BAC .08+	92%	100%
	BAC <.08	28%	84%
THC <i>only</i>			
	THC 5 ng/mL+	65%	99%
	THC <5 ng/mL	9%	94%

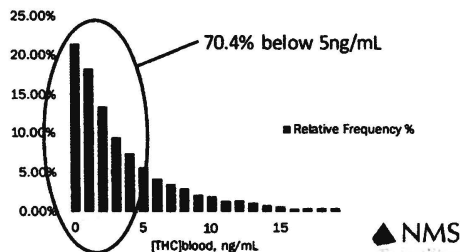
The 94% DWAI conviction rate for drivers who test below 5 ng/mL is convincing evidence that a 5 ng/mL level can prevent guilty drivers from conviction as shown by the 9% DUI conviction rate.

It turns out that most THC positive drivers arrested for DUI test below 5 ng/mL as shown by Figure 11 (Pennsylvania's NMS Labs). Unpublished data from other forensic laboratories in Colorado and Washington confirm that most THC positive drivers arrested for DUI in those states also test below 5 ng/mL.

Figure 11 Histogram of THC laboratory results from DUI arrests

Impact of 5ng/mL THC *per se* Law

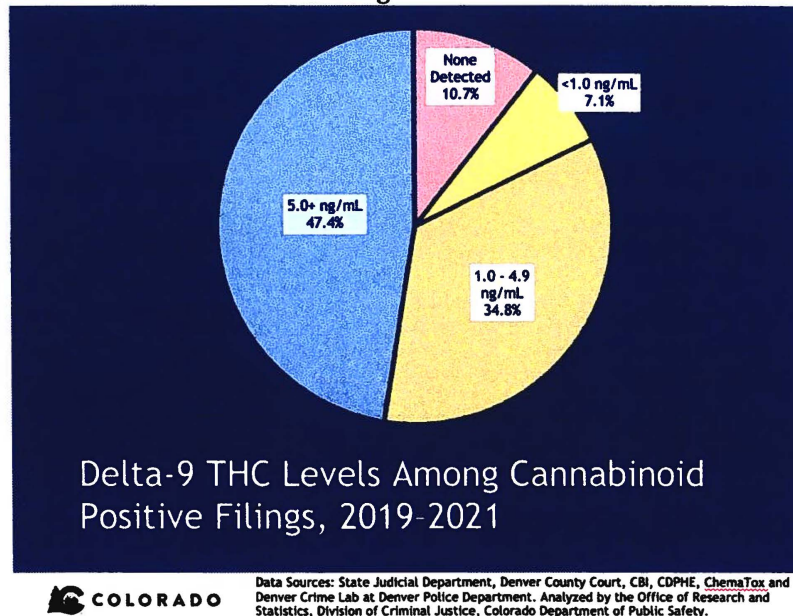
10,144 Marijuana DUID /DRE cases testing positive for THC and/or metab.



Source: Barry Logan, NMS Labs

Prosecutors should not and generally do not file a DUI case if they find the evidence is too weak to support a conviction. So, even though most THC positive arrests test below 5 ng/mL, most cases that are filed test above 5 ng/mL as shown in Figure 12.

Figure 12 THC levels of case filings



It's not just data – it's people

When the marijuana lobby says, "Marijuana hasn't killed anyone," they're talking about overdoses. They speak for their clients, not their victims. Marijuana does kill. Only the families of drugged driving victims can speak for them. Some do. Others mourn in silence.

Tanya and Adrian Guevarra

Tanya Guevarra, 25, and her 5-week-old son Adrian were driving to pick up a prescription in their hometown of Dacono, Colorado. Steven Ryan hit them head-on, killing Tanya instantly, but Adrian suffered several days before dying. Four hours elapsed before a blood sample was taken from Ryan. The blood was tested and confirmed at 4 ng/mL Δ^9 -THC.

Fortunately, this crash occurred before Colorado passed its 5 ng THC permissible limit law in 2013. Ryan accepted a plea agreement for one count of vehicular homicide due to DUI, saving him from the likelihood of being found guilty of two counts. Ryan's attorney argued during the sentencing hearing that the judge should be lenient, because Ryan wasn't even driving under the influence. After all, he was below the 5 ng THC limit that was then being considered by the legislature. The judge was having none of it, saying he could only enforce the laws that had been passed and signed into law.

Tanya's family and *DUID Victim Voices* testified very effectively at the sentencing hearing, which convinced the judge to levy a sentence of 10 years for the single count of vehicular homicide due to DUI (Class 3 felony). Ryan was released to community corrections shortly after Colorado's 5 ng law was passed.

Rosemary Tempel

Rosemary Tempel, RN, BSN, BC, CQIA was 56 years old at the time she was driving to work at Virginia Mason Hospital in downtown Seattle, WA. Speeding in the center turn lane, traveling in the opposite direction while under the influence of marijuana, Timothy Durden directed his Jeep directly into Rosemary's car. Durden's car catapulted over Rosemary's car – crushing her and breaking her neck, then lost the two front wheels and tumbled down the busy road resulting in an 8-car pileup. Upon uprighting Durden's vehicle, a Seattle police detective saw marijuana and multiple business cards to Seattle's Herbal Health Care Center marijuana dispensary fall from Durden's vehicle.

Durden volunteered to have his blood drawn 3 hours and 13 minutes after the incident. It was found to have 3.2 ng/ml THC.

During a pre-trial hearing, Judge Monica Benton threw out the marijuana blood evidence and thus the vehicular homicide (DUI) charge, stating she did not believe the Seattle PD

Drug Recognition Expert's (DRE) testimony. Benton also suppressed evidence of Durden's two previous DUI charges which were both plea bargained to reckless driving – citing them as not relevant and prejudicial. Durden's driving without auto insurance at the time of the incident, previous possession of controlled substances, and selling cocaine and marijuana to an undercover officer were all withheld from the jury. Judge Benton had previously permitted Durden to continue his use of marijuana while on probation for a domestic violence charge.

Durden was sentenced to 4.5 years following a jury conviction of vehicular homicide (reckless) + vehicular assault. He was released from prison more than 1.5 years early.

Rosemary's brother has become an effective advocate against drugged driving.

Peyton Knowlton



Kyle Couch's blood was drawn 2 hours after the crash that killed Peyton. Officers at the scene, found signs of impairment and cited Couch for DUI vehicular homicide. A DRE performed a complete DECP assessment, finding that Couch was incapable of safe driving, likely due to impairment by THC. The blood test revealed 1.5 ng/ml THC and an alcohol level below Colorado's legal limit. The THC level is what one would expect from a THC edible that Couch admitted to consuming earlier in the day.

The Class 3 felony charge was dropped when Couch pled guilty to careless driving resulting in death (a T1 traffic offense) which resulted in a 60-day jail sentence. He also pled guilty to using a false identity for purchase of alcohol and marijuana, resulting in an additional sequential 90-day sentence. That makes a total of 150 days in jail for killing an 8-year-old girl who just celebrated her 2nd grade graduation. Upon appeal, the jail sentence was dropped.

Brian and Erin Wood



Brian and Erin Wood were driving to a vacation home owned by Erin's parents on Whidbey Island, in Washington's Puget Sound.

Also on the road that evening were Jordyn Weichert and Samantha Bowling, driving an SUV with their boyfriends in the back seat. Weichert wanted to change her sweater and turned the wheel over to Bowling. Both women were at the wheel of the SUV when it crossed the center divider, flipped upside down, and was airborne as it went through Brian's windshield, killing him instantly. In the last seconds

of his life, Brian braked and swerved, in a futile attempt to avoid the collision. In so doing, he placed himself between the oncoming SUV and his wife, pregnant with their first child.

Investigators at the scene say that, had he not done so, Erin too would have been killed, along with their daughter. Erin was severely injured. Both men in the SUV's back seat, Jacob Quistorf and Fran Malloy were killed. Bowling broke her hip. Weichert was not injured.

As the SUV bounced down the highway, it disgorged clothing, un-belted passengers, and personal belongings, including heroin, methamphetamine, a drug weighing scale and packaging supplies, syringes, cooking foil, smoking pipes, and a 25-caliber automatic pistol. Responding paramedics strapped both women from the SUV onto backboards for transport to a local hospital. That prevented the responding Drug Recognition Expert from completing his assessment of their drug impairment. Nevertheless, the investigation concluded that both women were operating the SUV simultaneously, and both women were charged with three counts of vehicular homicide and one count of vehicular assault due to driving under the influence of drugs.

Subsequent lab tests confirmed methamphetamine and Carboxy-THC in both women as well as morphine (a heroin metabolite) in Weichert. Bowling pled guilty to three counts of vehicular homicide due to driving with disregard for the safety of others and agreed to a sentence of 61 months.

A jury trial found Weichert guilty of vehicular homicide and vehicular assault due to driving with disregard for the safety of others. The judge sentenced her to 96 months in prison – 32 months per homicide. Neither defendant was found guilty of DUI, despite the judge's comments during sentencing, "Drugs were a factor in this case. The fact that the defendants ingested drugs has increased the risk that they would engage in this reckless behavior that resulted in these deaths or injuries." Bowling was paroled after three years, Weichert after five years.

Victimized twice

All the above people were victimized twice. First, by a drugged driver. Second, by a justice system that is ill-equipped to deal with drugged driving.

Which leads us to the next section –

Enforcing drugged driving laws

All states prohibit not only drunk driving, but also drug-impaired driving. They do so in different ways. The most common offense is entitled Driving Under the Influence (DUI). Other terms may be used, including DWI (Driving While Impaired), DWAI (Driving While Ability Impaired), OUI (Operating Under the Influence), OWI (Operating While Intoxicated), OVI (Operating a Vehicle Under the Influence) or DUII (Driving Under the Influence of Intoxicants).

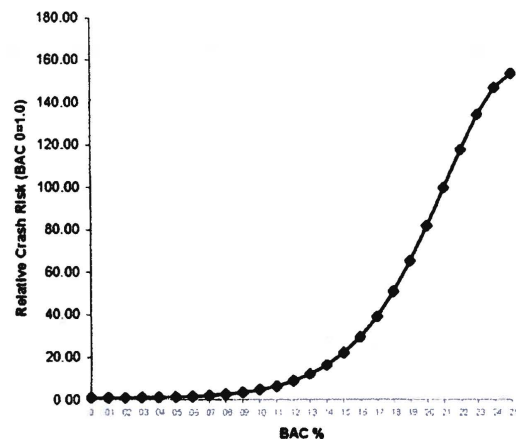
More important that the acronyms are the definitions of what DUI means. "Incapable of safe driving" is still used in some states but has gradually given way to definitions that may be easier to prosecute, like "Impaired to the slightest degree," or "less safe to drive." Most,

but not all states define their offenses statutorily. A few have one definition for drunk driving, and another for drugged driving. Several states statutorily do not define drunk driving DUI but do define drugged driving DUI.

All states prohibit both DUI and DUI *per se*. To convict of DUI, the state must prove that the driver was impaired to the level defined in statute or regulation. To convict of DUI *per se*, the state must merely prove that the driver had a BAC of at least .08 gm/dL (.05 in Utah). DUI *per se* is easier to prove than DUI.

Although politically determined DUI *per se* levels for alcohol are supported by scientific evidence such as Blomberg's graph in Figure 13⁵⁷, there are no drug *per se* levels that are supported by similar scientific evidence.

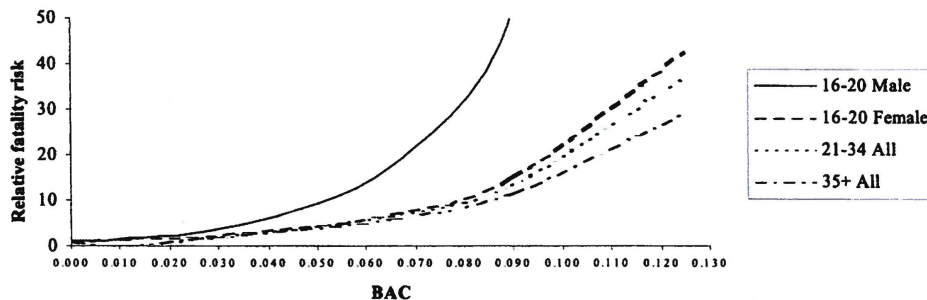
Figure 13 Crash risk as a function of BAC levels



Source: Evaluation of Utah's .05 Law, Blomberg et al.

Do not infer from Figure 13 that the crash risk curve represents all drivers. It does not, as shown by Zador's⁵⁸ finding in Figure 14.

Table 14. Relative risk as a function of BAC levels by age and sex



Source: DOT HS 809 050

The lack of correlation between crash risk and THC blood levels has not stopped states from establishing politically determined drug *per se* levels. The most common statute of this sort is the zero-tolerance statute that prohibits any level of illegal or intoxicating drugs in the blood of a driver. While not scientifically supportable, zero-tolerance statutes enjoy public support because they are sound public policy for illegal drugs, and there are exemptions granted for legal intoxicating drugs that are used according to a doctor's prescription.

Non-zero drug *per se* levels cannot reasonably be applied to all known intoxicating drugs even if they were supported by scientific research. Moreover, they would most likely be irrelevant in the more common cases of polydrug impairment since multiple drugs compound the driving impairment symptoms.

Without objective measures of impairment like evidentiary breath and/or blood tests for alcohol, proving drug impairment is a challenge. Determining whether a driver is impaired is similar in some ways to how a physician diagnoses an illness. A physician studies both symptoms and laboratory tests in making a diagnosis and determining a treatment plan. Police also rely upon symptoms and chemical tests to determine impairment and to prove impairment in court. Just as some disease diagnoses are straightforward and others are more challenging, effectiveness of impairment assessments vary depending upon the subject, impairing substance(s) and dose, symptoms, and of course, the diagnostician.

Symptoms of alcohol impairment are overt, and the chemical assays are definitive. Odor, bloodshot eyes, speech, behavior and balance are readily detected by even untrained observers. Horizontal Gaze Nystagmus is a validated⁵⁹ tool used by officers trained in Standardized Field Sobriety Tests to confirm alcohol impairment above 0.08 BAC. There is a very high correlation between BAC and levels of impairment⁶⁰. For THC, symptoms are much more subtle and chemical assays play more of a supporting role than a definitive role.

The most common tools used by police to document and prosecute impaired driving is the set of Standardized Field Sobriety Tests (SFSTs). They have been unofficially modified by some agencies to be more sensitive to THC impairment⁶¹. Yet, as Marcotte pointed out⁶², even modified SFSTs may be insufficient by themselves to denote THC impairment in drivers. Interviews with the offender and observations of both personal and driving behavior are critical additional parts of the evidence package.

The best tool we have now to confirm drug impairment is DECP, the Drug Evaluation and Classification Program administered by the International Association of Chiefs of Police (IACP). More than 8,000 DREs (Drug Recognition Experts) in the US are currently trained in DECP protocols. They are an excellent tool, but they are inadequate in terms of number, capability, legal support and public acceptance to equal the power of a scientifically supported drug *per se* law.

The DECP protocol has been validated in the laboratory⁶³ and in two field studies^{64 65}. The validation studies found that trained officers correctly identified the drug classes causing

impairment observations 80-90% of the time and rarely claimed that a study subject was impaired by a drug when no drug was found by laboratory assessment. In a Los Angeles field study⁶⁶ in only one of the 173 cases did an officer identify a subject as impaired when no drug or alcohol could be confirmed in the laboratory. The DRE protocol includes a laboratory assessment as step number 12 to prevent false positives from proceeding to conviction.

The three referenced DECP validation studies were performed before the program's parameters were formalized and subjected to oversight by the IACP. Some validation studies used urine rather than blood for confirmation, all drug classes were not studied in all validation studies, and neither field validation study performed laboratory tests on subjects considered by officers to be unimpaired (controls), which is necessary to identify false negatives. For these and other reasons, the validation studies themselves have been called into question⁶⁷. Nevertheless, the DECP program has been accepted by law enforcement in all 50 states, several other countries, and results have been determined to be admissible as valid scientific evidence in multiple court hearings.

DECP divided attention tests of walk and turn, one leg stand, modified Romberg balance, finger-to-nose as well as the eye tests for lack of convergence and rebound pupillary dilation are particularly sensitive to identify THC impairment^{68 69 70}.

Determining drug impairment, whether by use of interviews, observations, SFSTs and/or the DECP protocols is more difficult and less certain than determining guilt of DUI *per se* by laboratory data alone. Few symptomatic impairment assays can be performed on a driver injured in a drugged driving crash. A driver strapped onto a backboard awaiting transport to a hospital is unable to be assessed by any of the SFSTs or most of the DRE protocol steps. In those cases, law enforcement officials must rely principally upon interviews and an examination of driving behavior that caused the crash. In Washington state a DRE officer is precluded by the state Supreme Court from rendering an expert opinion in court unless all twelve DRE steps were followed, and in the order specified by the IACP, making expert opinions unavailable if the driver is injured. Other states have various other limitations on use of DRE opinions.

Nevertheless, relying upon our law enforcement professionals is all we have to enforce drugged driving laws. Unfortunately, all too often, that just isn't enough.

Incidentally, as difficult as it is for highly trained officers to identify drug impaired drivers, how can employers be expected to identify drug impaired employees? How about servers in "cannabis lounges?"

Conclusions

THC impairs drivers, causes crashes and kills people. The fact that the average driver impaired by THC is less dangerous than the average drunk driver is slight consolation –

they are still dangerous. Being less dangerous than the average drunk driver is a very low bar.

The universal alcohol DUI *per se* law provides a societal safety net. There is a very high probability that drunk drivers will be convicted. Drivers know that, which acts as a deterrent to drunk driving. True, it's proven to be an inadequate deterrent, but a deterrent, nonetheless.

There is no marijuana analog to alcohol's DUI *per se* limit. And there never will be. We have no technology to provide the safety net that we have for drunk drivers. Drivers know that fact. Alcohol's DUI deterrent does not exist for marijuana.

In Colorado, drugged driving is now half of DUI arrests, and most (~68%) drugged driving involves THC.

Even though marijuana is only quasi-legal (illegal at the Federal level, legal in most states in one form or another), we still have more chronic THC users than we have chronic alcohol users. And the difference between the two is growing rapidly.

Like other liberalization policies discussed relative to Figure 1, downclassification of marijuana would serve to accelerate that difference, creating more marijuana users, many of whom would contribute to an already untenable drugged driving problem.

We have no accepted objective measure of THC impairment or of impairment by polydrugs.

The poor conviction rate for marijuana-impaired drivers is not well known because Colorado is the only state that measures conviction rates by substance causing the DUI arrest. Colorado has not yet acted on the data available to it.

UNTIL AN OBJECTIVE THC DRIVING IMPAIRMENT ASSESSMENT TOOL IS AVAILABLE, IT IS IRRESPONSIBLE TO DOWNSCHEDULE MARIJUANA. The danger to public safety of further support to the marijuana industry is too high without such a safety net in place.

About the author:

Ed Wood, president of DUID Victim Voices has a B.S. degree in chemistry from Harvey Mudd College and an M.B.A. from the University of Colorado, Boulder. He retired as CEO of medical device company, COBE BCT, Inc., now Terumo BCT, Inc. His son Brian was killed by two drug-impaired drivers at the wheel of one vehicle (see page 21). After a disappointing and puzzling jury trial of one of the drivers, he spent years working with and learning from victims, prosecutors, defense attorneys, judges, toxicologists, legislators, state officials, and an international list of researchers and other specialists in his quest to learn the causes of this miscarriage of justice. He has published several peer-reviewed publications on the issue of drugged driving and has been a frequent speaker on the topic. Prompted by a recommendation from the Governors Highway Safety Association, he wrote the 2017 law requiring Colorado to begin collecting and reporting data on drug-impaired driving.

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CERTIFICATE OF SERVICE

I certify that this document was filed with the Court via the court's electronic filing system, on the 17th day of February, 2025, and an electronic copy was served on all counsel of record via the CM/ECF system on the same date. I further certify that I have mailed the foregoing document via first class mail, postage paid, to those parties or their counsel who are not registered through the CM/ECF system.

/s/Austin T. Brumbaugh

Austin T. Brumbaugh